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EDITED BY

LIONEL S. BEALE, M.B., F.R.S.,

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Mucous Tissue of the Umbilical Cord.

Let me now ask your attention to the anatomy of a peculiar connective tissue which has been particularly studied by Virchow, and on the structure of which he lays the greatest stress, for he states that in a good preparation, "a symmetrical network of cells is brought into view, which splits up the mass into such regular divisions that by means of the anastomoses which subsist between these cells throughout the whole of the umbilical cord, a uniform distribution of the nutritive juices throughout the whole of its substance is in this instance also rendered possible."

Fig. 12, Plate V, is a specimen of the "mucous tissue" from the umbilical cord, under a power of 130 diameters. The texture appears to be composed of delicate fibres with oval nuclei, which are for the most part arranged to form the boundaries of small circular spaces, in which are seen more delicate fibres arranged without regularity. The interspaces between the fibres are occupied with a transparent fluid.

In Fig. 13, some of the fibres and their nuclei are seen under a power of 700 diameters.

The preparations of this tissue which I have made exhibit a great number of the so-called fibre cells. In very many instances the continuity of the germinal matter with the *outer fibrous portion* of each elementary part is most distinct. I have not succeeded in demonstrating the appearance figured and described by Virchow. What appears to be a space or cavity in the centre of the elementary parts is really occupied with germinal matter, and the apparent tubes contain prolongations of this with the recently formed and soft fibrous tissue, which very readily breaks down. The arrangement of the fibrous tissue is shown in the drawing. It will be noticed that there is not the slightest resemblance between my drawing and Virchow's figures. (See pp. 98 and 100 of Dr. Chance's Translation.) It is impossible to represent in a wood engraving the extreme delicacy of the real fibres, but with this exception I think my drawing is a fair copy of the specimen.

Fig. 14 represents some of the muscular fibre cells which form a very thick layer around the arteries of the cord. The relation and mode of formation of the formed material in both structures are the same, but its properties are very different.

The so-called "mucous tissue" of the cord seems to be composed of a soft form of fibrous tissue which is produced in the

same manner as the formed material of other tissues. I have not been able to make out in it an arrangement of channels as Virchow has described. I cannot, therefore, agree with his statements with reference to the existence of a special canalicular system for the circulation of the nutrient juices in this tissue.

Bone.

Fig. 18, Plate VII, shows how the perfect and more permanent bone is produced by changes at the periosteal surface. The temporary imperfect bone is entirely replaced by the structure thus formed. Although in its general appearance my drawing is seen to resemble others which have been given, it will be found to differ from them in some most essential particulars. In the figures referred to, the cells are themselves seen to become stellate, while in my drawing the stellate appearance is shown to depend not upon any alteration in the form or position of the cells or nuclei, but merely upon the manner in which the calcareous matter is deposited in the formed material.

No stellate corpuscle has been produced, but the stellate appearance seems to result from the circumstance that the calcareous matter has been deposited in the matrix in such a manner as to leave intervals of a form more or less stellate. The reason of this will presently appear. The calcareous matter is at first deposited so as to form a network with nearly equal meshes. Each space contains an oval mass of living germinal matter and is the earliest condition of a lacuna. (Fig. 18, *d*.)

The elementary parts concerned in the formation of lacunæ in the above specimen are represented in different stages of growth in figs. 19, 20, 21, under a power of 1700 diameters.

Fig. 26 shows the manner in which the earthy matter is deposited in the matrix of cartilage. It is copied from a section of the temporal bone of a frog. Globules of earthy matter may be seen to form imperfect rings around the cartilage cells. The calcareous matter is always deposited in the matrix (formed material), at a point midway between adjacent "cells" that is in the oldest portion of the formed material of the cartilage. The deposition gradually proceeds from without inwards. The outer part of the germinal matter of the cell gradually undergoes conversion into matrix, which in its turn becomes impregnated with calcareous matter until only a small space remains in which the nucleus still exists.

Figs. 25 to 30 show these stages, and in many specimens, especially from the frog, rounded globules of calcareous matter which coalesce and undergo great change in form, can be demonstrated without difficulty in lacunæ in an advanced state of formation (fig. 29). Mr. Rainey has watched this process and seems to consider that molecular alterations in the earthy particles are the essential changes to which the formation of bone is due.

I have examined the process of ossification as it occurs in various animals with the aid of carmine, and have always been able to demonstrate masses of germinal matter in a position corresponding to the lacunal space. I believe these masses of germinal matter to be as necessary to the production of bone as they are to the formation of every other tissue, and feel certain they are constantly present, and that through their agency alone, osseous, as well as all other tissues, is formed. They are not directly concerned in the deposition of the calcareous matter, but the matrix in which this is deposited cannot be formed without them, and it is probable that by their instrumentality alone the regular circulation of fluids holding the calcareous matter in solution is maintained, and thus the extreme regularity with which the growth of the tissue occurs is ensured.

For some time after the first deposition of the calcareous matter in the formed material, very thin fragments of the bone torn away exhibit the appearance of fibres (a fact pointed out many years ago by Dr. Sharpey), in the substance of which globules have been deposited (fig. 31), but slowly the calcareous matter becomes more homogeneous, in consequence, probably, of changes occurring in its substance, and its more perfect incorporation with the organic matrix, and ultimately the hard mass appears even in texture, uniformly transparent, and penetrated everywhere by minute tubes.

It seems to me that these tubes are the altered spaces which are left between the calcareous globules originally deposited. They were at first triangular in outline, but gradually they have become altered by the filling up of the angles, until at last they become pores, the section of which is nearly circular.

From appearances I have seen in some preparations of the bones of the frog's skull (frontal, parietal), I feel sure that in this case the bone results from changes in the original cartilage. The nucleus of the cartilage cell remaining as the nucleus in the lacuna. The calcareous matter deposited in the matrix around a cartilage cell undergoes changes, probably slowly becomes incorporated with the organic matter, and gradually ceases to exhibit the appearance of being composed of separate

masses, and becomes more homogeneous. The spaces become canaliculi, and the mass at last assumes the structure of perfect bone.

For some time separate calcareous particles are seen within the outline of the lacunæ, which gradually diminishes in size as calcareous matter is deposited in the matrix from without inwards. Fig. 29 represents about one-third of the inner part of a recently-formed lacuna of the frog, magnified 1,700 diameters. A part of the nucleus is seen in the lower part of the drawing.

In the development of the long bones of mammalia, on the other hand, it is equally certain that the spongy, imperfectly formed bone at first developed is gradually removed, and gives place to new bony tissue of a more perfect structure not formed from cartilage, while, as is well known, there are examples of the formation of bone without the existence of cartilage at any period, in the case of certain bones of the cranium.

Kölliker considers that the capsule of the cartilage cell and the matrix, become impregnated with calcareous matter, while the granular cell corresponding to the primordial utricle of the vegetable cell and with the endoplast of Mr. Huxley, remains within unaltered. He thinks that the canaliculi extend through the matrix by resorption.

Virchow regards bone as consisting of cells and an intercellular substance, and he considers the canaliculi to be processes which grow from the cells.

In the following MS. note, copied from page 417 of Dr. Chance's translation, he expresses himself very clearly as to the manner in which processes are formed from cells. "The cartilage cells (and the same holds good of the marrow cells), during ossification throw out processes (become jagged) in the same way that connective tissue corpuscles, which are also originally round, do, both physiologically and pathologically. These processes which in the case of the cartilage cells are generally formed after, but in that of the marrow cells frequently before, calcification has taken place, bore their way into the intercellular substance, like *the villi of the chorion do into the mucous membrane and into the vessel of the uterus*, or like the Pacchionian granulations (glands) of the pia mater of the brain into (and occasionally *through*) the calvarium." Again, "The cells which thus result from the proliferation of the periosteal corpuscles are converted into bone corpuscles exactly in the way I described when speaking of the marrow. In the neighbourhood of the surface of the bone the intercellular substance grows dense and becomes almost cartilaginous, the cells *throw out*

processes, become stellate, and at last the calcification of the intercellular substance ensues."

There are few points in minute anatomy upon which such different views have been advanced as the one under consideration, and you cannot fail to notice that observers differ not only in the explanations and opinions they have put forward, but that there are irreconcilable differences in their statements of the facts.

Although many observers have described and somewhat faintly expressed in their drawings the growth of the processes referred to, all agree that they are most difficult to see in healthy growing bone. My own observations compel me to oppose the statements generally made with regard to these processes. As far as I have been able to see, neither the cartilage cell, nor the medullary cell, nor the periosteal cell, nor indeed any cell in the organism becomes stellate by the "shooting-out process." That cartilage and the other "cells" may become angular is perfectly true, and that a few little projections may be seen from different parts of their surface is also true, but these projections and angles have nothing to do with the formation of canaliculi. The appearance is exceptional instead of being constant, and a lacuna with numerous canaliculi may be produced without the existence of an angular cell at all. The mass of germinal matter is oval from the period it first existed as a separate object to the time its nucleus is seen in the lacuna. Into each lacuna forty or fifty or more canaliculi open, and these communicate with those of adjacent lacunæ. Surely, if these were formed in the manner described we ought to be able to demonstrate something like this during the formation of the lacunæ, but nothing of the sort has been seen, and the warmest advocates of the theory have only been able to observe a very faint indication of the arrangement which they believe actually exists. Their drawings only show these processes projecting a very short distance from the cells, and no one, I believe, ever pretends to have seen processes from two neighbouring cells in process of communicating with each other, as exists constantly in the perfect canaliculi of bone. It is not only very difficult to conceive such channels formed by an out-growth, but it is inconsistent with what is generally observed, to suppose that channels are scooped out in a tissue which has just been formed. The tissue *during its formation* requires channels for the transmission of nutrient matter just as much as after its formation is complete.

If the canaliculi were formed as described it is quite impossible that every observer should have failed to see the prolonga-

tions of the cell undergoing development and coalescing with those of neighbouring cells. The extremities of these tubes which were gradually extending through the matrix would be rounded, and would contain germinal matter which would absorb the solid matrix, and thus the tube would extend through its substance. No such appearance has ever been seen. The canaliculi are no more processes of the cell which bore their way through the hard material than the tubes which are found in the masses of secondary deposits in the hard walls of certain vegetable cells are processes of the germinal matter in the centre of the cell.

Again, it is very difficult to understand why tubes growing centrifugally from adjacent cells should not grow outward, at least at first, in direct lines, and reach each other by the shortest cuts, while, according to my view, as the deposition of the calcareous matter commences always at the point where two elementary parts coalesce, where the oldest part of the formed material is situated, it is easy to see how the canaliculi, or spaces left, must be continuous with each other, and their tortuous course also receives explanation from the fact, that the particles first deposited become globules before the process of ossification is far advanced.

It may be said, if you please, that the growing matter extending from a spore of mildew bores its way into the soft material, at the expense of which it grows, but here this soft material is clearly appropriated by the mildew, and becomes converted into the germinal matter of the plant, but this process is totally different from that by which canaliculi are produced.

Myeloid cells (Plate VII, fig. 24) are a good specimen of the so-called myeloid cells from one of the cancelli of the bone of the great toe. Two or three of the masses are elongated and much bent. These I believe might afterwards become ossified and form the spiculæ of bone which form the imperfect septa between the cancelli. Around these are many small granular cells, and it is interesting to notice the fact, that while the first structures are of a dark-red colour the latter are scarcely tinged with the carmine, although both have been exposed to its influence in the same way. The first is growing actively, the last is comparatively inactive, and there can be no doubt that it is being gradually removed as the former structure advances. What remains will become the medulla. The so-called myeloid cells are not peculiar to the cancelli and the medullary membrane of bones, but they are also formed in the periosteum. Under ordinary circumstances many of them gradually become

converted into bone, but in disease they increase in number rapidly, producing a soft, spongy structure which only undergoes very imperfect ossification or receives no calcareous deposit at all. In these so-called mycloid cells I have not been able to distinguish a cell wall. Each mass is composed of a number of small oval elementary parts, each of which consists of an oval mass of germinal matter which is faintly coloured, while the nucleus is coloured dark-red with carmine. The germinal matter gradually undergoes conversion into a soft formed material externally, which increases in thickness. Afterwards the nucleus diminishes in size. In some cases the formed material exhibits a somewhat fibrous appearance.

Dentine.

There are few anatomical questions which have given rise to more controversy, than the structure and mode of formation of the dentine, and the very last writer on the subject, M. Lent, describes the dentinal canals as consisting of direct processes of the whole dentinal cells. "The matrix of the dentine is not formed of the dentine cells, but is a secretion of these cells and of the tooth pulp, in other words, an intercellular substance.*" Now, Mr. Tomes has shown that the dentinal tubes are occupied with a soft solid structure which may be seen projecting in the form of solid processes from the broken ends of the dentinal tubes. The truth of these observations has, however, been doubted by several observers. I have been able to verify Mr. Tomes' statements as to the dentinal tubes being occupied with this soft structure, and now send round a preparation in which this material has been coloured red with carmine, and is most clearly demonstrated (No. 49). The dentinal "tubes" of a *living tooth* are never empty; indeed they are not tubes, nor are they canals for the transmission of nutrient substances dissolved in fluid, but they contain a soft solid substance, the central portion of which is in a state of active vitality.

Imagine for a moment one of the soft nuclear fibres of tendon surrounded with a matrix impregnated with calcareous matter and you will form, I believe, a good idea of the structure of the "dentinal tube" and its contents.

The wall of the tube with the matter between the tubes correspond to the "wall" of an ordinary cell, or to this and the intercellular substance (my *formed material*), and the contents of the tube to the granular cell contents with the nuclei (my

* Kölliker's Manual of Microscopic Anatomy, page 307.

germinal matter). If you look at the tissue of the pulp just beneath the surface of the dentine you find a number of oval masses of germinal matter coloured intensely red by carmine. These are nearly equidistant and separated from each other by a certain quantity of material which is only very faintly coloured, and in cases when the solution was not very strong it remained colourless. This colourless matrix is continuous with the *intertubular dentinal tissue*, while the intensely red germinal matter, or rather a prolongation from it, extends into the dentinal tubes. The germinal matter with a thin layer of soft and imperfect formed material is easily detached from the formed material by which it is surrounded, and its continuity with the dentinal tubes may often be torn away, (prep. 50). The whole then appears as an oval mass (cell) with a prolongation as it were into the dentinal tube. (Fig. 32, *a*, Plate VIII).

The general description given of the manner in which these dentinal tubes *open* upon the walls of the pulp cavity is certainly true, but it is true only of the dry tooth. In the living tooth a prolongation from one of the "cells" on the surface of the pulp is prolonged into each tube. The tubes cannot, therefore, serve as mere conduits for nutrient fluids which transude through the walls of the vessels, and are supposed to pass along the tubes to the outer part of the tooth. Moreover, in some cases certain of the so-called dentinal tubes are completely solid, the tube being obliterated (fig. 36). These points receive a ready explanation from a careful consideration of the facts I have brought forward.

The specimens which have been sent round prove, I think, that the formation of the dentine and the so-called tubes, is effected in a much more simple manner than is usually believed. The elongated masses of germinal matter first of all produce *formed material*, which gradually increases as in other cases, upon the outer surface of the germinal matter. The formed material of the adjacent elementary parts is continuous, and calcareous matter is first deposited in the oldest part of this formed material. The calcareous matter appears in the form of small globules, which gradually increase in size, and often several coalesce. Thus the formed material, or matrix, of the dentine becomes calcified. (Fig. 32, *a*).

Not unfrequently, however, several of the calcareous globules increase in such a way as to inclose a portion of uncalcified matrix. This being, as it were, imprisoned by hard impermeable structure retains its soft primitive state. If the tooth be dried the soft matrix in these spaces shrinks and air rushes in. Thus the appearance known as "globular dentine"

is produced, and the reason why uncalcified tubes are seen traversing these spaces becomes manifest.

After the matrix of the dentine is calcified the germinal matter still slowly undergoes conversion into formed material, which in its turn becomes impregnated with calcareous matter. The germinal matter diminishes in thickness. The formed material is produced more slowly after the general basis has been laid down, and hence the dentine immediately surrounding the tube seems to be distinct from that lying in the intervals between the tubes. The germinal matter gradually shrinks from the outer part of the dentine (the oldest portion) towards the pulp-cavity, where these changes still go on. In the dry tooth the same fact may be expressed by saying that the narrowest part of the dental tubes is at the circumference of the dentine, and this part was the first formed; the widest part is that which is in contact with the pulp, and this is composed of dentine most recently developed. Internal to this is a narrow layer, the formed material of which is not yet calcified.

Figs. 33, 34, 35, 36, 37, are copied from specimens taken from different parts of the dentine. They show the varying diameter of the tubes, and are confirmatory of the observations just made.

The appearances I have described can only be demonstrated in perfectly fresh teeth, which have been placed in carmine solution very soon after extraction.

The principal changes in such a tissue as dentine seem to consist of the conversion of germinal matter into formed material, and the impregnation of this formed material with calcareous matter, rapidly at first, but more slowly as the quantity of calcareous matter increases. In the adult, the remains of the germinal matter slowly undergo conversion into formed material, and this slowly becomes impregnated with calcareous cells. In old age, although the pulp is very much reduced, this conversion is not complete, and a certain amount of germinal matter still remains in the tubes and in the pulp cavity from which dentine might have been produced.

Tissue with Stellate Cells.

Stellate tissue on surface of crusta petrosa.—Upon the surface of the fang of the tooth in contact with the crusta petrosa is a tissue of a very interesting structure, which takes part in the formation of the cementum. It is composed entirely of what may be described as branching cells (elementary parts), the processes of which anastomose freely with each other. It is from

this tissue that the crusta petrosa is formed; but I allude to it here because it is a most perfect example of a tissue consisting entirely of cells, the cavities of which *communicate with each other by tubes.* The stellate cells are here as distinct as they are in the pith of the rush. But do these cells and tubes merely constitute an elaborate system of channels for the distribution of nutrient material to the tissue which intervenes between them? This tissue, it may be remarked, grows very slowly; it is a very low simple form of tissue, and probably requires but very little nutrient matter. If the above view is adopted it must be admitted that the means for nourishing the structure are far more elaborate than would be expected, supposing the conclusion is accepted that there ought to be a constant relation between the activity of change in a tissue and the mechanism for bringing new matter to the elementary parts and carrying off the effete material from them.

Neither does it appear that all these bodies become lacunæ of the cementum. The stellate cells just described for the most part have not more than from ten to twelve processes or tubes projecting from them, while many of the lacunæ of the cementum have as many as thirty or forty, hence these tubes are certainly not an early stage of the canaliculi, and the cells cannot become lacunæ simply by the deposition of calcareous matter in the intervening matrix or intercellular substance.

This stellate tissue on the surface of the fang nevertheless undergoes calcification. The process of calcification may be seen to take place in specimen 52. The processes of the stellate masses become narrower and narrower until, the germinal matter, which they contained, having undergone conversion into formed material, they cease to be coloured by carmine. (Fig. 43, Plate IX). They now look like roundish, highly refracting cords, which are colourless, and connect the several stellate masses of dark-red germinal matter with each other. Here and there in the intervals between these processes small globules of calcareous matter have been deposited, and these increase and completely surround the cord-like processes. Many of the processes gradually assume the character of the surrounding matrix, disappear as distinct cords, and like the rest of the tissue become impregnated with calcareous matter.

Many of the stellate masses of germinal matter (cells) shrink and disappear in consequence of the same changes having occurred. Others remain with their processes, and their nuclei possibly remain as the nuclei of the lacunæ which are irregularly distributed through the cementum; but I cannot express

myself positively on this point. It is certain that all the cells do not become lacunæ, for in this tissue there are half-a-dozen stellate cells to one lacuna in the cementum, and many of the canaliculi are five times as long as these tubes. Are these processes tubes? This question would doubtless be answered in affirmative by every one who examined the tissue long after death, but during life they contain a solid, or semi-solid, substance corresponding to that which occupies the so-called dentinal tubes. They contain portions of the germinal matter which is undergoing conversion into formed material, and the situations in which these tubes existed are the last portions of the formed material to undergo calcification.

This is precisely the same change which takes place in the calcification of the dentine, the only difference being in the forms which the masses of germinal matter assume in the first instance. It need hardly be remarked, that cementum, as it ordinarily exists upon the fangs of the human teeth, differs from true bone in its greater degree of hardness, in the small number and irregular arrangement of its lacunæ, and in the absence of the arrangement for its absorption and reproduction. It is a more permanent but less perfect tissue than bone.

Stellate fibre cells from the aorta, Preparation 43, is a very thin section of the circular coat of the aorta, coloured by soaking in carmine, showing large stellate muscular fibre cells. It will be interesting to compare this with the tissue upon the fang of the tooth. The radiating processes seen in this specimen are clearly not tubular; the large stellate elementary parts were very readily separated from each other. I hope you will particularly remark that in this specimen the central part of each is very darkly coloured by carmine; external to this the structure is coloured, but the colour becomes fainter in the most external portions, and the outermost part of each fibre and its prolongations, are perfectly colourless. The fibrous character of the tissue is sufficiently manifest. As in many other cases, the germinal matter is here seen in the centre of the mass, and is gradually giving rise to the production of formed material, the oldest and that which is perfectly formed being at the greatest distance from the central mass, while that which was but recently germinal matter, and is now in a transition state, is continuous with it. The latter is slightly coloured with carmine while the perfectly developed formed material is not coloured at all. (Fig. 44).

Let me, in conclusion, offer a few general observations upon the formation of bone, dentine, and the beautiful stellate tissues, represented in figs. 43 and 44.

The early formation of bone is not the least like the early formation of a tissue with stellate cells. In the former the so-called cells (masses of germinal matter with formed material externally) are round or oval at every period of their development, and may be separated from each other without difficulty. In the stellate tissue the masses of germinal matter are connected together for a considerable period of their existence; at first the points of communication are wide, but they gradually become narrower and narrower as the distances increase, and at last they are reduced to narrow processes which at length undergo conversion into formed material. The germinal matter of the different masses may communicate through these processes up to a certain period, but gradually they become more solid, and then the masses are distinct, but still connected to each other by narrow cord-like processes.

The nutrient material passes to the germinal matter of each mass, and to that prolonged to each *through* the formed material which is deposited in the intervals. In some stellate tissues fluid only exists in this situation, which is afterwards absorbed, leaving spaces between the walls of the tubes into which air passes.

The dentinal tubes, and the tubes of the stellate tissues, therefore, do not correspond to the canaliculi of bone. Their counterpart is seen in many vegetable tissues (Vol. II, Plate XII, figs. 1*k*, 2), at the point where the separate masses of germinal matter are connected together; while the channels corresponding to the canaliculi are the pores through the secondary deposits in vegetable cells. (Vol. II, Plate XV, figs. 2, 3).

The stellate cells are stellate from the very beginning. The bone cell is never stellate at any period of its existence. The tubes in the first case contain germinal matter. The tubes in bone are merely spaces left between the particles of calcareous matter which are deposited in the matrix, and for this reason do not exist in the formed material of bone or cartilage prior to the deposition of calcareous matter. They are present when calcareous matter is deposited in cartilage. The dentinal tubes correspond to the processes from, and the cavities of, the stellate cells, but they differ entirely from the canaliculi of bone. The so-called tubes in the stellate tissue and in dentine are no more tubes than the space filled with germinal matter in an elementary part—say of the cuticle—is a cavity. Spaces remain if the germinal matter is removed; but during life these so-called tubes and spaces are occupied with the most important part of the whole structure,—the living, active-growing germinal

matter. The canaliculi of bone, therefore, do not correspond to the above tubes or spaces; they do not contain at any period of their formation germinal matter. They are mere channels left during the deposition of calcareous particles in the formed material.

These channels in bone are, no doubt, subservient in a very important degree to the rapid changes which occur in this hard tissue. The bone tissue could not be so rapidly formed or so quickly removed if it were not freely permeated by canals. In dentine the formed material becomes much more slowly impregnated with calcareous matter and incorporated with the organic matter, so that a very hard, even, and very permanent structure results in which pores exist only in certain parts, especially in the granular layer of the dentine.

In all cases the formed material is impregnated with calcareous matter from without inwards. The necessity for the existence of bone at a very early period of development, the gradual alteration in the size of the bones during the growth of the body, and the changes in their form seem to be incompatible with a mode of development like that by which dentine is produced.

While Virchow has been led by his researches to the conclusion that nutrient tubes exist in connexion with cells in soft tissues, the results of the observations I have recorded in this lecture, have compelled me to conclude that such tubes do not exist in soft tissues as tubes for the transmission of nutrient material, and that even the so-called dentinal tubes are not nutrient canals; while it appears that the canaliculi of bone which are of this nature do not correspond to the dentinal tubes, or to the communicating system of channels in a tissue composed of stellate branching cells, but are mere spaces left during the rapid formation of a tissue impermeable to fluids.

Lecture VII.

Connective Tissue, continued.—Intercellular Substance (formed Material).—Cells or Nuclei (Germinal matter).—Areolar or Connective Tissue Corpuscles and the system of communicating nutrient channels.—Areolar Tissue.—Nerves in Skin of Mouse.—Mucous Membrane of Fauces.—Pericardium, its nerves and ganglia.—Voluntary Muscle.—General remarks on Areolar Tissue.—Conclusion.

Although the connective tissues are generally described as composed of *cells* and *intercellular substance,* I brought forward a number of facts which seem strongly opposed to the view generally entertained, and the preparations which were passed round have, I trust, at least, convinced you that the explanation I have advanced is not incompatible with the facts which were observed. I hold that the so-called intercellular substance exactly corresponds to the cell wall, and like it was formed from germinal matter.

I have tried to show that at an early period of the development of all these tissues there is no proper intercellular substance; and by examining the same tissue at various stages of its growth one cannot but come to the conclusion that the structure, which in the fully developed tissue seems to lie between the cells, formed at an earlier period part of the substance of the cells; that an elementary part of adult cartilage or fibrous tissue, for instance, consists of germinal matter, and formed material upon which the peculiar characters of the tissue entirely depend; and that the proportion of formed material gradually increases as the age of each elementary part

advances, so that the masses of germinal matter become separated from each other by greater distances. As a general rule the formed material of the constituent elementary parts of connective tissues is continuous, and it is not possible to isolate each elementary part as in epithelium and such structures; but in certain cases even this can be effected, and the analogy becomes so distinct that it seems impossible to separate the class of connective tissues from epithelial structures on the ground of any mere differences of structure or mode of growth.

I propose now to consider the bearing of the anatomical points I endeavoured to prove in my last lecture upon the question of connective tissue generally. I shall first allude to the intercellular substance, and afterwards consider the nature of the "cells" or their representatives in this series of tissues.

Intercellular Substance (Formed Material).

Many observers in the present day seem to consider that the intercellular substance is of far higher importance than the cells or nuclei embedded in it. This *matrix* or *intercellular substance* has been supposed, too, to play a most important part in morbid changes. It is considered that the intercellular substance possesses active powers. It may be at first composed of a soft and perfectly clear and homogeneous substance, but it subsequently undergoes important changes in its properties. By some observers it is supposed to become *differentiated* into various substances by virtue of its own inherent powers, while others attribute the changes which occur to the action of the cells. It is asserted that in all connective tissues, cells and an intercellular substance can be satisfactorily demonstrated. In white fibrous tissue the yellow elastic tissue is said to be developed from, and is the representative of, the cellular element, while the white fibrillated tissue is regarded as the intercellular substance which by many is supposed to be formed independently of cells. This part of the question has already been considered in page 74.

It appears, then, that some observers consider that the intercellular substance is simply deposited from the blood, and perhaps somewhat modified by the action of the cells between which it is formed, while by other authorities the intercellular substance itself is believed to possess inherent powers of growth, assimilation, and conversion.

If the intercellular substance of white fibrous tissue and cartilage is merely deposited from the blood by a process akin to crystallization, some substances from which gelatine or

chondrin could be obtained should exist in that fluid. But no such substance has ever been detected.

If, on the other hand, this intercellular substance possesses formative power, and by its own inherent powers can convert certain nutrient materials into matter possessing the same properties as itself, what end is served by the germinal matter which is so constant? And why are these masses so much more numerous in young than in fully developed cartilage? The object fulfilled by the growth of such textures as fibrous tissue and cartilage is the formation of the so-called intercellular substance upon which all the properties of the tissue depend. It is in this that the peculiar properties of firmness, strength, or elasticity reside; for the cells (masses of germinal matter) certainly do not possess any such characters. If, then, this substance can increase itself, wherefore are the cells present at all? The universality of the presence of germinal matter is meaningless, and its abundance in all rapidly-growing tissues, its gradual diminution as the formed material increases, and the deterioration in the properties of the tissue constantly associated with its abnormal increase or with its death, are facts which do not receive explanation.

If both cells and intercellular substance require to be nourished, what regulates the exact supply so that neither increases upon the domains of the other? And how is it that the selected powers of each are exactly balanced?

The investing membrane of a spore or a portion of the stem of mildew, or other simple plant, corresponds to the so-called intercellular matrix of tendon, cartilage, &c. If the latter grows by selecting substances from the nutrient fluid which bathes it, the former must be produced by selecting substances from the fluid which surrounds it. But I have shown that the inner germinal matter may diminish as the cell-wall increases in thickness, and that while there are many examples of germinal matter which is not surrounded with a distinct cell-wall or intercellular substance, there is not an instance of the latter existing in a growing state without the former. When the mildew grows, so far from the outer material or cell-wall increasing in thickness, it becomes thinner (Vol. II, Plate XII, fig. 1*d*, *l*, *m*, *n*). It is the germinal matter within which increases. The germinal matter alone grows, and the more rapidly it increases the thinner is the external membrane (formed material) found to be. A small portion of the germinal matter of the mildew placed under favourable conditions will grow and will produce the formed material or cell-wall, but the cell-wall from which the germinal matter has been removed will

not grow under any circumstances whatever. The envelope or cell-wall exhibits the same characters after the death of the germinal matter as it possessed during its life, but the germinal matter undergoes very rapid changes after death: it soon becomes liquefied, passes into decomposition, and various chemical compounds are formed which did not exist during its life, which, in fact, are incompatible with its life and with the changes which occur while it is alive.

Cells or Nuclei (Germinal Matter).

The germinal matter of connective tissues differs remarkably in its arrangement, as has been stated. Reference should be made to Plates IV, V, VI, and VII, in which the germinal matter is shown embedded in the formed material of tendon, cartilage, bone, and dentine. Although in many cases in the adult tissue the proportion of formed material (intercellular substance) is very great, this is not the case in the young tissue. At an early period of development of all these textures, germinal matter is present in considerable proportion. I have endeavoured to show how the formed material is produced, and have brought forward numerous observations in support of the view that the intercellular substance results from changes in the germinal matter, and that these textures, like all others, originate from this substance.

Those who consider the so-called nucleus as the least important and least constant part of the tissue will perhaps answer the above remarks by the assertion that nuclei are not to be detected in all tissues, and by calling attention to observations in which these nuclei are stated to be vacuoles in a homogeneous structure. I have already stated that they are much more numerous in many tissues than is generally supposed, and are to be demonstrated only by the action of carmine and certain other colouring matters. With regard to the so-called *vacuoles* in young tissues generally, let me remark that the clear material occupying these spaces is the substance I have termed germinal matter, which becomes coloured red by carmine.

In young vegetable tissues the term vacuole is applied to spaces containing a transparent material which occupies the same position as that in which the primordial utricle is afterwards found. This transparent material and the primordial utricle are both coloured by carmine, and both consist of germinal matter. The manner in which secondary deposits occur in the substance of this germinal matter has been referred to in page 263, Vol. II.

As I have shown that the material (germinal matter) coloured red by carmine in cartilage and tendon exactly corresponds to that in epithelium, and that neither cartilage, epithelium, nor any other structure exists in a growing state without it, surely I am justified in the inference that it is *essential* to these tissues. If cartilage could be formed without germinal matter the cell-wall could be produced independently of it. There is no more reason for believing that cartilage or fibrous tissue can be produced from a nutrient fluid without the agency of active living matter than that this living matter can be precipitated from a fluid composed of a solution of inanimate matter.

The contents of cells are easily removed from the investing membrane, or from the walls of the cavity in which they are contained, because the structure which lies between the germinal matter and the perfectly-developed formed material, although continuous in the natural state of the parts with both, is exceedingly soft. It is no longer composed of particles like the germinal matter which are held together as a viscid coherent mass, nor is it yet sufficiently firm to possess the powers of resistance resident in the fully-developed formed material. The substance in this situation is in a transition state, and separation very easily takes place at this point. After death changes commence very soon in this imperfect formed material.

Areolar or Connective Tissue Corpuscles, and their System of Communicating Nutrient Channels.

The term *areolar* or *connective tissue corpuscle*, has been applied to the corresponding structures in several different tissues. In certain textures where I can prove that nerves and capillaries are abundant, a vast number of these connective tissue corpuscles are said to exist. The nature of the so-called areolar tissue corpuscles in the skin and other tissues will be discussed shortly.

Supposing the relation I have described as existing between the germinal matter and formed material of tissues to be true, and the arguments I have advanced sound, it follows that if this term is applied to the elementary parts of bone, cartilage, and tendon, it must also be applied to those of muscle, nerve, the epithelium of the skin, glands, &c., for the germinal matter of cartilage makes cartilage, that of tendon tendon, and those of muscle, nerve, epithelium, &c., produce the formed material which exhibits the peculiar endowments characteristic of these tissues.

With regard to the existence of spaces and tubes, it has been observed that, under certain circumstances, spaces are undoubtedly to be demonstrated in the substance of various tissues, and connecting these there are tubes. They do not exist, however, as spaces and tubes for the conveyance of nutrient fluids in the living tissue. Both are the result either of a change occurring in the course of nature, or are artificially produced by the alteration of their contents by chemical reagents, the action of water, &c. In the first case the tissue is dying or dead, but the last is the explanation when tubes and spaces are said to have been demonstrated by the passage of air or coloured fluid in tissue, which was recently in an active growing state; except in the case of bone and analogous structures, where tubes are present. In short, these so-called spaces and tubes in soft tissues actually contain the active living part of the tissue. It is here that the inanimate nourishment commences its life, and passes through various changes until its place is occupied by new matter, and it has become firm and hard, and perhaps comparatively permanent, as tissue. The tubes and spaces really contain living spherical particles in all stages of being, from the recently animated matter to the particles becoming tissue. The soft living material is, of course, easily destroyed, soon decays after death and leaves spaces and tubes, but during life these are occupied with the only matter of the tissue which can produce new matter, the material on which the growth, the nutrition, in short, the life of the whole depends.

In pathological alterations the germinal matter of cuticle or of cartilage will undergo multiplication in precisely the same manner as the germinal matter of a tissue, the several masses of which communicate with each other by tubes.

It has been shown that in some tissues, as cartilage, the masses of germinal matter are entirely separated from each other by formed material, while in others as tendon they are continuous. Gradually, however, these channels of communication in many tissues become completely closed up, although their position continues to be marked by a line exhibiting a different amount of refractive power to the rest of the formed material. How is this fact to be accounted for on the supposition that these are mere tubes for the transmission of nutrient fluids?

In tissues which are rendered impermeable by the precipitation of calcareous matter in the formed material, and which are at the same time quickly produced and quickly removed, channels must exist for the transmission of fluids to and from the germinal matter. But in soft, permeable textures such

tubes are not required as fluids circulate freely through the interstices of the tissue or formed material.

These corpuscles and communicating tubes which are regarded by Virchow as belonging to an extensive nutrient system of tubes and cavities, exhibit very different characters in closely allied tissues. Although present in periosteum and perichondrium, they are absent in permanent and temporary cartilage. The bundles of white fibrous tissue contain, it is admitted, a vast number of them, while the substance of the elementary fibre of muscle in immediate continuity with the tendon is, at least in many instances, destitute of anything like such an arrangement; although the first tissue is one in which the nutritive changes are slight, while in the latter they are admitted to be very active.

The mucous tissue of the cord, according to Virchow, consists almost entirely of these anastomosing tubes, and there a most elaborate system for the conveyance of nutrient juices is said to exist, although with the exception of a little imperfectly formed fibrous tissue and viscid matter there appears nothing in this texture requiring nourishment. There is no secretion, and the changes occurring in such a texture must be slow. (See Page 81, and Plate V, figs. 12, 13).

They (connective tissue corpuscles) are found in connection with the capillaries of the ciliary process of the eye and those of the Malpighian bodies of the kidney in greater number than with capillaries generally. They are numerous in the cornea, in fibrous tissue, and in inflammatory lymph, and although present in some forms of cartilage they are absent in others. It is not easy to understand why they should be very numerous in some tissues situated quite close to vessels, and absent in others separated a considerable distance from the vessels. Why they should be present in some textures which undergo slight change, and absent in others where important nutritive changes must be continually and rapidly taking place. Why the soft, permeable, temporary, mucous tissue of the cord should require a wonderful nutrient system of this kind, while the hard and much less permeable cartilage is destitute of any such arrangement. Why the "cells" should be arranged in linear series in tendon and fascia, stellate in periosteum, perichondrium, and fibro-cartilage. Why the *radiating* tubes should be so distinct and so large in the mucous tissue of the cord, periosteum, and certain forms of fibro-cartilage, and so difficult of demonstration in tendon, and so narrow that the advocates of the doctrine are compelled to admit that in adult tendon the indisputably solid fibres of yellow elastic tissue are their representatives, and are

forced to support their argument with the statement, that at least at an early period of development the fibres of yellow elastic tissue are hollow? If the young white fibrous tissue, which is comparatively freely supplied with vessels, requires a special system of nutrient canals we should expect to find such canals at least persistent in the adult where the tissue is farther removed from the blood, instead of which they appear to become occluded as the necessity for their existence increases. Moreover, I have adduced instances of white fibrous tissue with parallel fibres, in which no fibres of yellow elastic tissue could be demonstrated, although the arrangement of the nuclei was the same as in other forms of this structure.

It is to be observed, however, that the stellate arrangement does exist in cases where a tissue is gradually increasing for a considerable period of time in all directions. In the cartilage of which the semicircular canals are composed in the frog, the masses of germinal matter do communicate, while in the adjacent cartilage of the temporal bone no such arrangement exists. In periosteum and in the areolar tissue of the skin, which extend in all directions, the arrangement is stellate, while in tendon, which extends chiefly in two directions, it is linear. In voluntary muscles of the system of vertebrate animals generally (with some exceptions) the masses of germinal matter are separate, while in the muscular fibre of the heart they are connected, forming lines which occupy the centre of the fibre; and I might bring forward many other facts which receive something like an explanation according to the view I have proposed, but which cannot be accounted for on the other theory. It is very hard to believe that different forms of cartilage are developed and nourished in a totally different manner. This question, however, requires further investigation.

I have endeavoured to prove, that in nutrition inanimate matter becomes germinal matter, while the latter is converted into formed material, and thus in certain cases the production of new-formed material makes up for the amount which is disintegrated. The rate at which these processes are respectively carried on will determine the increase or diminution of the texture and will materially influence its consistence and period of existence. I consider that always in nutrition the pabulum first becomes germinal matter, and that germinal matter is, therefore, always present in tissues which receive nutrient material, and not only so, but that it varies in quantity according to the activity of the nutrient process, or in other words, according to the rapidity of change in the tissue.

Certain forms of Areolar or Connective Tissue.

The areolar or connective tissue in connection with many of the higher tissues of the body appears as a delicate fibrous texture, in which the direction of the fibres is not uniform, or as a delicate transparent web, in which granules and irregular fibres are here and there seen, destitute of nuclei, and of any form of yellow elastic tissue, or associated with one or both of these latter structures. These forms are to be distinguished from the well-defined bundles of white and yellow fibrous tissue which possess nuclei, and which are found in the corium and in other situations. The structure we are now considering has been spoken of as indeterminate or indefinite connective tissue. You find it in papillæ, as in those of the tongue and skin, in connection with vessels, nerve fibres, and muscular fibres, between the follicles of glands, the uriniferous tubes, and in the brain and spinal cord, and in many other situations. It is often considered as a bond of union between different textures, and as a support to higher tissues, but it must be remembered that at an early period of development, when the tissues and parts of organs are very soft, and seem to be in greatest need of support, there is no indefinite connective tissue. Moreover, it must be quite obvious that in such an organ as the kidney the different structures support each other. The uriniferous tubes support the vessels which lie between them, and *vice versâ*.

By some it is asserted that this form of connective tissue contains cells or nuclei, while others deny this, and assert that even the higher forms of white fibrous tissue are produced independently of these structures. I have endeavoured to disprove the truth of the latter assertion, but I feel quite sure that the former statement is true. I have seen certain forms, both of white and yellow fibrous tissue, which are destitute of nuclei. The mode of formation of these structures will be presently discussed.

At an early period of development this form of connective tissue is absent. There are only traces of it in the fœtus at the seventh or eighth month, but it is found in increased quantity in the tissues of the child, and in still greater proportion in the adult. In some situations I think I have demonstrated that it increases as age advances, but at the same time it undergoes condensation, and therefore occupies less space. In disease it is often increased in situations where only traces are present in health, and it is found in situations

where it is absent in the normal state. It is frequently present in large quantity in situations from which higher tissues have disappeared.

During the process of development tissues which serve but a temporary purpose are constantly being replaced by the growth of higher and more permanent structures. The complex tissue which exists in the adult is represented in the embryo by a much more simple type, which is removed and replaced often by several series of textures before a tissue like that of the adult is produced. The tissues are not developed in their permanent form, and do not simply increase as the body grows, but those textures which perform certain functions in the adult, are represented in the embryo by tissues which perform corresponding, but not exactly similar offices. Not only have the permanent glands certain temporary substitutes, differing from them in important points, but the structure of the different tissues, muscle, nerve, bone, &c., becomes modified as development proceeds, until the permanent type of structure is reached. At the sixth or seventh month of intrauterine life it is not possible to trace the representatives of all the adult structures, in the finger, for instance; most active changes are occurring, and it is quite evident that the newly-formed tissues are growing and encroaching upon structures which attained their maximum of development at an earlier period. The nerve fibres and vessels alter as much as any other tissues. A space which in a given position in the fœtal finger contains only capillaries and terminal nerve fibres, will, at a later period, contain arteries, veins, and nerve trunks, as well as capillaries and terminal branches, and later still, will contain, and perhaps be entirely occupied with, large arterial and venous trunks, and bundles of trunks of nerve fibres. The Pacinian corpuscles, the sweat glands, and the papillæ are all to be seen, but their structures and relations are very different when development is more advanced. There are no sudden changes, no sudden transitions from one tissue to its immediate successor, but the processes take place very gradually, and the temporary tissues slowly give place to their more perfect and more permanent successors. When the perfect type has been attained, new tissue of the same kind is formed, while the old is gradually removed, and in some textures these changes proceed so quickly that elementary parts of every age are to be seen, from the earliest embryonic state to the perfect structure, and from this to the wasted remains, which enable us to complete the history of the changes which occur.

When an organ which is destined to remain throughout life has been developed, special provision is found to exist whereby the removal of its component elementary organs and the development and growth of new ones is provided for. At every period of life elementary parts and organs are to be met with in every stage of formation, and it sometimes happens that the elementary organs of the kidney, for instance, are impaired when in an embryonic state. No evidence of any change may appear for a long time, but at length the time arrives when these elementary organs should have attained their perfect state, and should be ready to perform the work of the organ. Their predecessors being worn out, and no new parts developed to take their place, the work cannot be performed, and in the case of an organ like the kidney, liver, or brain, death must result.

The fibrous capsules of organs are not composed of a form of connective tissue like fascia, merely required for protecting or supporting the structure which it encloses, but veins and lymphatics are often abundantly distributed in its substance; and in carefully prepared specimens it is not uncommon to meet with portions of the altered structure of the gland even in the very substance of the capsule. The gland substance not unfrequently adheres to the capsule so firmly that in tearing it off portions of the secreting structure are torn away with it. In certain morbid changes in the structure this adhesion is much more intimate than in the healthy state. This fact, and many others which I must not stop to discuss at present, are explained upon the view that the oldest portions of the gland structure lie in contact with the capsule, and are absorbed in this situation, certain portions which are incapable of removal in a soluble form remaining, and thus contributing to increase the thickness of the capsule.

The arteries, veins, capillaries, and nerves, like other tissues, are perpetually undergoing change, and a certain amount of connective tissue seems to be always associated with these structures. It sometimes exists in such large quantities that the important tissue lies completely hidden and embedded in it; while in young small animals, as in the young white mouse, it is in some situations not to be demonstrated. As the animal advances in age, however, this tissue appears. Delicate fibres of connective tissue are found in immediate continuity with some of the finer branches of the nerves, as I have already mentioned.

Upon the external surface of a nerve trunk there is often a considerable quantity of fibrous tissue, which is in connection

with, or at any rate adheres to, the nerves. It seems as if this had resulted from the development of masses of germinal matter similar to those which produce the nerves. The truth seems to be, that germinal matter, which in the normal state would produce a high tissue like muscle or nerve, may, under other circumstances, give rise to the formation of a degraded structure, not possessing the high endowments characteristic of these tissues, and assuming the form of the simplest and lowest normal textures.

Let me now pass round a few specimens which illustrate some of the points I have mentioned, and I think you will find that many discrepancies and conflicting statements will be explained, if we study this widely distributed form of connective tissue from the point of view suggested by the remarks I have made.

Nerves in the Skin of the Mouse.

Preparation 53 is the skin of the white mouse, seen from below. The bulbs of the hair and the sebaceous follicles arranged in rows are very prominent objects, and between them and around them in every part of the specimen are seen small arteries, veins, capillaries, and bundles of nerve fibres. As you alter the focus you see nerve fibres at every plane; several may be traced to the hair bulbs which they encircle. A nervous plexus of the most intricate character, in which it is possible to follow an individual fibre for a considerable distance, is seen in this preparation. As the magnifying power is increased a greater number of fibres come into view. Connected with the capillaries, arteries, and veins, are numerous oval nuclei, and nuclei much resembling them are seen at very short intervals along the nerve fibres. Nuclei connected with fat vesicles are also observed. Besides, there are some small spherical bodies, which I believe are either white blood corpuscles in the capillaries or lymph corpuscles. In the crowd of nuclei all the above can be recognized, but besides them there are also nuclei in connection with the fibrous tissue of the true skin. Of all these separate masses of germinal matter, or nuclei, those connected with nerve fibres and capillaries can be readily distinguished. These alone form lines which branch, the branching being of a different character in the nerves and capillaries. In some parts of the specimen the capillaries are injected, and the nuclei in their walls can be most positively distinguished from those connected with the nerves. The latter, which are very numerous, are found in connection with all nerve fibres, and

are very numerous, and situated at very short distances from each other in the terminal branches. They are not mere swellings or varicosities, but oval masses of germinal matter, which are coloured by carmine, and are as necessary to the life of the nerve fibre as those of cartilage, or fibrous tissue, or epithelium, or muscular fibre are integral parts of those structures, and necessary to their existence. The nerve fibres are very numerous in every part of the specimen, and as the fibrous tissue of the skin grows as the nerves increase, the latter gradually become embedded in it, and are with great difficulty followed out in ordinary specimens. In this preparation, bands composed of three or four trunks are seen to divide, some of the fibres passing to an adjacent band, so that a most complicated plexus is formed, and it is exceedingly difficult to find a fibre which is undoubtedly single. As the power is increased, fibres are resolved into two or three, which were not visible by the powers in ordinary use, (two to three hundred diameters).

Mucous Membrane of Fauces.

There are few structures more beautiful than those displayed in a thin section, near the surface, of a sensitive mucous membrane from man or the higher animals; but it is so difficult to demonstrate the arrangement of the delicate nervous plexuses in these tissues that the anatomy of these structures has not been fully described. Immediately beneath the epithelium of the mucous membrane of the palate, fauces, and pharynx of man, there exists the most intricate plexus of nerve fibres that can be conceived. Exceedingly thin sections are required, and I have found practically that these may be more easily obtained from the mucous membrane covering the epiglottis than from that of other parts. After the parts have been injected with Prussian blue fluid, the epiglottis is removed, treated with carmine, and preserved in glycerine. The mucous membrane adheres pretty firmly to the cartilage beneath. With a very sharp thin-bladed knife the layer of epithelium may be removed in such a manner that the surface of the subjacent membrane is completely exposed in some places, while in others a very thin section of the deepest layers of epithelium remains, and here and there a thin section from the surface of the mucous membrane itself will have been removed. Next, the thinnest possible horizontal section is removed parallel to the cut even surface, and transferred to glycerine. After being carefully covered with very thin glass, the specimen is examined with a power of from five to eight hundred diameters. In favourable

specimens an arrangement of nerve fibres so wonderful is brought into view, that the observer will examine the specimen again and again before he can convince himself that what he seems to see, is real. Flattened bands, composed of from two to five or six nerve fibres, are seen crossing the field in every direction, and in the small intervals between them, finer and still finer branches are brought into view by careful focusing. Some of the fibres are of very large size, but others, in their general appearance, very closely resemble the gray, or gelatinous, nerve fibres. It is possible that some few of the fibres observed may be muscular fibres of the mucous membrane, but there cannot be the least doubt, that by far the majority are nerve fibres, which form a most intricate interlacement immediately beneath the epithelium. Moreover, it is to be noticed that there are at least two kinds of nerve fibres in this situation. Although many of the finest fibres are probably the terminal ramifications of branches which are thicker at a distance from their termination, there can be no doubt that the widest fibres are distinct from these altogether, and are not in any way connected with them.

Here and there the nerve fibres may be seen to divide, but from the great number present it is often difficult to isolate an individual fibre in which the division may be seen very distinctly. I believe the divisions of dark-bordered nerve fibres occur pretty frequently. In the palate of the frog, however, where the nerves are very numerous, but not nearly so abundant as in the human subject, this point is demonstrated without great difficulty.

In specimens from which the epithelium has been removed by gentle scraping instead of by section, little papillæ may be seen, and into these nerve fibres may be traced. The branches are seen to be bent upon each other in several places, and may be said to form a loop, the fibres of which are bent sharply at short intervals, so that the body of the papilla is twice or three times as wide as its neck where the nerve fibres pass into it. Several of these papillæ, as far as I could ascertain, were destitute of capillary vessels, but it is possible that very fine capillaries may have existed, which, from not having been injected, were not demonstrable. The papillæ above described may be regarded as a more simple form of the tactile corpuscle present in the papillæ of the fingers, toes, lips, &c. Beneath the plexus, above described, are larger bundles of nerve fibres, with vessels and much yellow elastic tissue. Connected with these nerve fibres are many ganglion cells, and here and there a microscopic ganglion.

The existence of small ganglia and ganglion cells in connexion with the nerves of this and some other mucous membranes is a point of great interest and importance, especially when considered in connexion with their absence beneath the skin. Beneath the mucous membrane of the pharynx and palate of the frog, ganglia and ganglion cells are present in great number, but, have never seen one connected with the cutaneous nerves.

Oval nuclei or masses of germinal matter are very numerous, and are seen at very short intervals in all the nerve fibres. They are most numerous in connexion with the finest nerve fibres. They are also numerous on the vessels, as in other parts. In a carelessly prepared specimen nothing but these numerous nuclei, which appear to be embedded in a slightly fibrous intermediate structure, are observed. Not a nerve fibre is to be made out in some specimens prepared in the ordinary manner, and were I even to alter the density of the glycerine in the specimens I have passed round (Preparations 54 and 55), the appearance, now so distinct, would at once be lost.

In some places, from carelessness in manipulation, the distinctness of the nerve fibres is lost, and in these situations the nuclei are seen in connexion with very fine fibres, not altered by acetic acid, and resembling in all respects yellow elastic tissue. In the external coats of arteries and in the pericardium, similar appearances have been observed, and from these and other facts, which I shall allude to in a separate communication, I think that certain forms of yellow elastic tissue are the remains of nerve fibres, and perhaps other structures which were in a state of activity at an earlier period of life.

Pericardium, its Nerves and Ganglia.

Preparation 56 is the pericardium of the human fœtus at the seventh month removed from the surface of the heart. The capillaries have been injected with Prussian blue. The bundles of nerve fibres are seen crossing the field and dividing and subdividing into smaller bundles, so that a network of nerve fibres with wide meshes is formed. Numerous oval nuclei are observed at short intervals in connection with all the fibres forming these bundles. The distribution of the finer branches cannot be made out definitely because the fibres, except when a great number are placed together, appear perfectly transparent. Fibres of white and yellow fibrous tissue

can be detected in this specimen, but the quantity of connective tissue present, is very small compared with that existing in the adult pericardium.

In Preparation 57, ganglion cells and large bundles of gray, gelatinous, nerve fibres are seen. These have been dissected or from the pericardium of the ox. Three separate ganglion cells situated at the side of the nerve fibre have been placed in the field, and each ganglion cell is surrounded with bands of nerve fibres resembling those of which the trunk of the nerve is composed. Nuclei exactly resembling those in the fibres are seen embedded in the substance of the ganglion. (Plate IX, figs. 40, 41, 42).

From this and other appearances one cannot but conclude that the fibres are continuous with the ganglion cells, and are developed from them. The nuclei being formed in the substance of the ganglion cell, as well as subsequently by the division of those connected with the fibres. I believe that the nerve fibre with its nuclei may be regarded almost as an extended ganglion cell. Each ganglion cell is connected with several nerve fibres, and the so-called capsule of these cells, generally described as consisting of areolar tissue, is really composed of nerve fibres which wind round a considerable part of the circumference of the cell, and then divide into bundles, which pass in different directions. The nuclei which are described as the nuclei of the areolar tissue capsule are the nuclei of the fibres and exactly resemble those in unquestionable nerve fibres. Those nerve fibres embedded in the substance of the pericardium seem to contain no tubular or dark bordered nerve fibres, (fibres with the white substance of Schwann).

On the external portion of these bundles of nerve fibres in the adult and surrounding the ganglia, a considerable quantity of areolar or connective tissue generally exists, and very commonly the quantity is so great that the nerve fibres and ganglia are obscured by it. Preparation 58 is a microscopic ganglion embedded in the areolar tissue, just outside the base of the aorta near its origin, from the human subject, and Preparation 59 is a ganglion embedded in the adipose tissue from the left ventricle of the heart of the pig. The ganglia are numerous in the grooves between auricles and ventricles in the pig's heart, but they are so completely embedded in the adipose tissue that it is only by making thin sections one after the other that they can be discovered. I have also found numerous microscopic ganglia in corresponding situations in the human heart.

These preparations prove that the pericardium contains numerous very fine bundles of nerve fibres which form a net-

work situated at the deep aspect of the fibrous pericardium, and on the surface of the muscular fibres. The branches are much more numerous in and near the longitudinal groove of the heart, and the grooves between auricles and ventricles, but many can be demonstrated over the general surface of the ventricles. At short intervals bundles can be seen to dip down in the spaces in which the vessels also pass, and these from their transparency are soon lost amongst the muscular fibres. Numerous microscopic ganglia, resembling those of the sympathetic, are connected with many of these nerve fibres. In some cases, collections of ganglion cells are seen at the side of the nerve fibre, and in many instances two or three ganglion cells can be made out in the very substance of the trunk. These microscopic ganglia are demonstrated without difficulty and in immense number, in properly prepared hearts, but from the fact that most of them are embedded in adipose and in areolar tissue, they are very liable to be overlooked. They are most numerous at the base of the heart in the grooves between the auricles and ventricles, in the longitudinal grooves, and in the areolar tissue at the base of the large arteries, and in that surrounding the arteries themselves.

In the muscular substance of the heart, the fine branches of the nerves may be followed. Their general disposition resembles that in voluntary muscle, and, as the nuclei of the muscular fibres of the heart are in the very centre of the fibre, there is no fear of mistaking these for the nuclei of the nerve fibre. Many nerve fibres are distributed to the vessels, but by far the greater number certainly ramify on the surface of the muscular fibres. It is impossible to demonstrate these latter points unless the vessels have been, in the first instance, carefully injected with transparent fluid.

The preparations I have shown you compel me to differ from the general opinions now entertained, with reference to the nature of the so-called gelatinous, or gray, fibres. The distribution of these fibres seen in the pericardium, their connection with the ganglia, their constant appearance, the numerous nuclei connected with them, are all incompatible with the notion of their consisting merely of bundles of connective tissue. I can very easily show that many of these fibres are the only fibres connected with most unquestionable ganglion cells, and those who still maintain such fibres to be connective tissue, will, I think, find it very difficult to account for the presence of the ganglia in the number in which they are found in connection with this supposed fibrous tissue. I hold with Remak, and with Todd and Bowman, in this country, that

these gray fibres are veritable nerve fibres, and must be altogether removed from the connective tissue series; moreover, I must add in connection with this question that the branches of almost all, if not of all, nerves near their termination partake of the characters of the gray, or gelatinous, fibres.*

It must be borne in mind, that ganglia are much more abundantly distributed in the body than is generally supposed. Besides the well known sympathetic ganglia, visible to the unaided eye, microscopic ganglia of the same kind are very numerous, and in many of the trunks of the nerve fibres distributed to internal organs, small collections of ganglion cells, and even a single cell, are not uncommonly seen. Connected with the nerves in the palate of the frog are numerous ganglion cells, and I have found several in connection with the nerves distributed to the vessels of the same animal. They are found in the nerves distributed to all the viscera.

My researches on this subject are not yet sufficiently extensive, to enable me to express myself positively on this point, but I think it will prove that the only fibres connected with these round or oval ganglion cells of the sympathetic system, are the gray, or gelatinous, fibres. I have already shown that the oval nuclei are more abundant in fibres of which the trunks of the sympathetic are composed, than in other nerve fibres. Arguing from the inference deduced from observations upon the distribution of the nuclei in nerves generally, that they are the structures by which nerves are brought into relation with other tissues, the gray fibres and ganglia connected with them must be regarded as belonging to a nervous system which forms a complicated network, the branches of which extend to every part of the body, and which contains numerous centres presiding over the action of certain parts, but connected with other centres of this system in such a manner that the action of the whole is harmonized. Many of the sympathetic ganglia are connected with the cerebro-spinal system of nerves, but perhaps not so that the sympathetic can be said to *arise* from any part as from a centre. The experiments of Budge and Waller, and others, however, favour this view. I believe that from any part of one of the gray fibres, branches may grow which will place the parts to which it is distributed under the influence of the ganglia with which the nerves are connected. For instance, suppose a certain number of these fibres distributed to an artery, which gradually becomes larger, and from which an increasing number of branches proceeds. Every one of these will be supplied with

* On the Distribution of Nerves to the Voluntary Muscles.—Phil. Trans., 1860.

nerve fibres which will grow from the original bundle. In proportion as these branches increase the trunk and the ganglion, or ganglia connected with it, will increase. The nuclei of these fibres like those of all nerves near their distribution, undergo division and subdivision, and thus new fibres are formed according to the requirements of the part. You cannot separate a small band of gray fibres into separate individual fibres, nor can you divide the terminal branches of a cerebro-spinal nerve into distinct and separate fibres. Many of the finest fibres exhibit an indication of being composed of two or more, and this division seems to be continually going on in the peripheral branches of all nerves, and occurs in the trunks of the sympathetic system. Time will not permit me to dwell longer on this important question, but I hope to work it out shortly more in detail.

Voluntary Muscle.

Connective tissue exists between the elementary muscular fibres of the voluntary muscle of man and animals, and it has been considered as a constant structure, and subservient to certain important purposes, in this situation. The proportion of this connective tissue varies greatly in the voluntary muscles of different animals, and in those of the same animal at different ages. During the early period of development of muscle this connective tissue is not observable, and in the muscles of small animals, such as the mouse, only traces are to be demonstrated. The elementary fibres of the muscles of the young mouse seem to be quite destitute of connective tissue. On the surfaces of the elementary fibres of all voluntary muscles, at all periods of life, are a number of oval corpuscles or nuclei, and these are found in cases where very much connective tissue is observed, and also when no traces of this structure can be found. They are generally considered to be nuclei of the areolar or connective tissue, and are the bodies regarded as "connective tissue corpuscles."

No. 61 is a preparation showing the muscular fibres of the diaphragm of a young white mouse with their nerves, capillaries, and the numerous nuclei connected with them. The preparation is destitute of connective tissue, and all the corpuscles are connected with the capillaries, which are injected, with the nerve fibres, or with the muscular tissue itself.

General Remarks on Areolar Tissue.

A certain form of connective tissue not unfrequently results from the imperfect development of elementary parts from which a much higher tissue might have been produced.

In No. 44, some of the bundles of muscular fibre cells at the edge of the uterus of the mouse are seen, and those situated most externally are observed to differ from those in the more central part of the bundle. The formed material of these marginal elementary parts presents the appearance of ordinary fibrous tissue. A corresponding fact is observed with regard to the bundles of gray nerve fibres. The nuclei situated at the outer part of the bundle do not produce nerve fibres, but they give rise to the formation of a kind of connective tissue only. Up to a certain period of their existence nerve fibres might have been produced, but as a sufficient number had been developed, these marginal cells degenerated and led to the production only of a low form of tissue.

I have shown that fibres of connective tissue are very often connected with the terminal branches of nerve fibres, and this is especially the case in old tissues which are abundantly supplied with nerves. This point can be demonstrated in the frog's tongue to such an extent that it would not, I think, be possible to pronounce in certain cases, if a given fibre were in a state of functional activity as an integral part of the nervous system, or were merely a degenerated nerve fibre no longer active, and consisting of what might fairly be termed a form of connective tissue. The question can, however, always be determined by the presence or absence of the little oval nuclei or masses of germinal matter.

In many instances, I have been able to prove that these fibres in connexion with active nerve fibres were not acted upon by acetic acid, and beneath the plexus of nerves on the surface of the mucous membrane of the epiglottis were numerous parallel fibres exhibiting the reaction and general characters of yellow elastic tissue, and amongst the undoubted nerve fibres were fibres of the same description destitute of nuclei. Similar appearances have been observed in the papillæ of the human skin and tongue. It would seem, then, that by the alteration of nerves and capillary vessels, certain forms of 'connective tissue' are produced, and this has been observed in many different situations and in different animals, man, mouse, cat, frog, and others.

In the dura mater, the coats of small veins have been seen gradually thickening, until they were converted into solid bundles of fibrous tissue, and many have been seen with an exceedingly narrow cavity in the centre corresponding to the calibre of the vessel.

The alteration of nerve fibres into fibrous tissue has been very carefully watched in many localities. In the human organism the sole difficulty in following out the distribution of the nerves arises from this cause. Fibrous tissue also forms the remains of many other structures, in fact, the variety of this tissue which we are now considering is composed of the remains of various structures which cannot be entirely removed by absorption. The areolar tissue between the ultimate follicles of glands, that which surrounds vessels and nerves, and the fibrous tissue of which the so-called capsule of certain organs, liver, kidney, spleen, &c., are all of this nature. No wonder that in man, whose tissues pass through so many stages before he arrives at maturity, and in whom such active changes occur after this period, there should be a large amount of this structure. This form of fibrous tissue is absent in the embryo at an early period, exists in very small quantity in the young child, and the proportion gradually increases as age advances. In small animals there is less than there is in large animals, and in young animals there is less than in old animals. In creatures of the simplest organization, whose tissues are, so to say, embryonic throughout the whole period of their existence, there is none. In the higher animals whose tissues pass through so many phases before they attain their perfect form, there is a large quantity. A form of connective or areolar tissue is the result of certain degenerative processes occurring in higher tissues. It may result from changes occurring in vessels, nerves, and muscles. In various glandular organs which have undergone degeneration, a form of fibrous tissue remains behind. In cirrhosis of the liver, I believe the fibrous matter which is present results not from the effusion and fibrillation of lymph, but is simply the remains of the degenerated capillaries and ducts. In livers in this condition, vessels and shrunken secreting structure, can always be demonstrated in the substance of the so-called fibrous tissue. The same remarks also apply to the kidney in certain cases of disease, and to other glandular organs. The structure of inflammatory lymph has been already described. This gradually undergoes a process of condensation and a form of fibrous tissue at last results.

I must now make a few remarks upon certain fallacious

appearances which may be produced by the mode of preparing specimens of healthy tissues, and which may easily be mistaken for fibrous tissue. I have already adverted to this matter in my first lecture; I have seen the smaller blood-vessels, both arteries and veins, stretched in one part of their course so that the transparent injection was pressed out of the transparent tube, while its continuity with the other parts containing the blue injection was perfectly certain. Had I seen the stretched portion alone, I should have affirmed most positively that it was a form of areolar tissue, and the nuclei which belonged to the structure forming the coats of the vessels might have been considered to be the nuclei of the areolar tissue.

Delicate nerve fibres when stretched and pressed could not be distinguished from connective tissue. Under the same circumstances, capillary vessels and the membranous walls of ducts may be set down as 'areolar or connective tissue.'

It would seem, then, that there are—

1. Certain forms both of white and yellow fibrous tissue which are produced directly from germinal matter as other tissues, and in which masses of germinal matter may be demonstrated at every period of life.

2. Certain forms which may be regarded as the residue of higher tissues which have ceased to discharge active functions.

3. Certain forms of fibrous tissue (indefinite connective tissue), as in the papillæ of touch and taste, which result from changes having occurred in the terminal branches of the nerve fibres.

4. Certain forms of fibrous tissue, resulting from degeneration occurring in the course of disease (abnormal).

5. An appearance of fibrous tissue produced by pressure, crumpling, and stretching of nerves, capillaries, and other tissues.

You will have gathered from the observations I made when the last preparations were sent round, that I consider, for instance, in a structure like skin, that a number of bodies, taking part in the formation of special tissues, have been dismissed under the term 'connective tissue corpuscles.' The following bodies, composed of germinal matter and generally termed nuclei, are certainly present:—1. Nuclei of nerves. 2. Nuclei of capillaries. 3. Nuclei of white fibrous tissue. 4. Nuclei of yellow fibrous tissue. 5. Nuclei of fat cells. 6. Lymph, and white blood, corpuscles. In certain papillæ all the nuclei present may be shown to belong to nerves and capillary vessels, and between the elementary muscular fibres

of the young mouse this is also strictly true. I do not think that in such situations there are any corpuscles which could properly be called areolar tissue corpuscles, nor have I succeeded in obtaining any facts which would favour the view that there are corpuscles of any kind distinct from the 'cells' or 'nuclei' (germinal matter) of the tissue, which perform special offices connected with the nutrition of these higher tissues.

General Remarks and Summary of Conclusions.

In this course of lectures I have endeavoured to prove that the changes which more especially distinguish living structures from lifeless matter, take place in the substance I have termed *germinal matter* and in this alone. The particles of which this is composed after passing through certain definite stages of existence, undergo conversion into the peculiar substance or substances they were destined to produce. It is the germinal matter alone which is capable of *forming, producing* and *converting*. The matter external to it (cell wall, intercellular substance or fluid) has *been formed* or *produced*, and it may be changed, but it has no power to *produce* structure or to alter itself.

There are many objections to the use of the term 'cell' as indicating the elementary unit of structure. The cell-wall is not constant although it is absolutely necessary to the existence and action of the 'cell,' that is, in the sense in which this word is ordinarily used. There are comparatively few instances in which a true vesicle exists at all.

Every living structure, and every elementary part that is living, is composed of matter which is *forming* and matter which is *formed*—germinal matter and formed material. The term cell is short and convenient and if the definition usually given were modified, I think it would possess advantages over the term 'elementary part.' We might give the word a much more general signification and say that a 'cell' is composed of matter in two states which I have described under the terms germinal matter and formed material.

It appeared to me that great confusion would have resulted if I had attempted to show when describing various structures the exact parts which according to the ordinary nomenclature corresponded to my 'germinal matter' and 'formed material'

and I have therefore purposely omitted to discuss the question at all in detail. It may, however, be well to state now that in some cases the *germinal matter* corresponds to the 'nucleus,' in others to the 'nucleus and cell-contents,' in others to the matter lying between the 'cell-wall,' and certain of the 'cell-contents;' while the *formed material*, in some cases corresponds exactly to the 'cell-wall' only, in others to the 'cell-wall and part of the cell-contents,' in others to the 'intercellular substance,' and in other instances to the fluid or viscid material which separates the several 'cells, nuclei or corpuscles,' from each other. It may be remarked—

That the 'nucleus' of the frog's blood-corpuscle is *germinal matter;* the external red portion (cell-wall and coloured contents), *formed material.*

That the white blood corpuscle, the lymph and chyle corpuscle, and the pus and mucous corpuscle, are composed entirely of *germinal matter*, with a very thin layer of *formed material;* the viscid matter or mucus between the mucous corpuscles is *formed material.*

That the 'nucleus' of an epithelial cell of mucous membrane, or of the cuticle is *germinal matter;* in a fully formed 'cell' the outer part, 'cell-wall and cell-contents' consists of *formed material.*

That the 'cell-wall' of a fat-cell or of a starch-holding-cell is *formed material;* the 'nucleus' of the former, and the 'primordial utricle' of the latter, are *germinal matter;* while the fat and the starch are the secondary deposits produced by changes occurring in particles of germinal matter in the central part of the mass.

I have chosen the terms 'germinal matter' and 'formed material' because they serve to express the essentially different nature of the two forms of matter of which every elementary living structure is composed at the time it is under observation. I do not think that it is possible for any living particle to exist without being composed of matter in these two states,—matter capable under favourable circumstances of producing germs from which new germs may be developed infinitely,—and matter which once possessed this power but which has been formed or converted into a substance endowed with certain peculiar and important properties, it is true, but now totally destitute of the power of producing matter like itself, reproduction, &c.

It may be remarked that by the use of these terms alone, the changes taking place in the development, growth, and nutrition of tissues in health as well as in disease may be

described. I have endeavoured to study and describe *actions* and *changes* rather than to give names and definitions to structures which exist at any given period, but which are in a state of constant though gradual and perhaps very slow change. To aim at giving a history of the changes which occur seems to me more likely to lead to useful results than to attempt to define arbitrarily the limits of structures between which there is in nature no observable line of demarcation. In many cases the *germinal matter* passes gradually into the *formed material*, and it would be impossible to describe these by using the ordinary terms,—for there are no means by which we could determine positively which part of the structure was *cell-wall*, and which *cell-contents*. I may, however, be permitted to say that I am quite ready to modify the terms employed, in any way which may be likely to render them more convenient or more useful.

No attempt has been made to define exactly what is an *individual*. It seems to me that as the several component parts of the organism of the higher animals are dependent upon each other for their existence, we cannot look upon any one elementary part as an *independent growing living structure*. The conditions necessary for its existence are such that it cannot live when detached. On the other hand the contents (germinal matter) of what appears to be an elementary part (cell) of a simple fungus may be divided perhaps into many thousand particles, every one of which is capable of existing independently, of growing infinitely, and of producing a structure resembling that from which it has sprung. I have brought forward evidence favourable to the view that living particles exist which are far too minute to be seen by any magnifying powers which have yet been made. Again, there are many instances in which division can be carried to a certain degree of minuteness with the production of a multitude of living particles, each one of which grows into a structure resembling that of which it was but a small part. But if the structure be divided into more minute particles the death of all results. The simpler the conditions necessary for existence the more independent are the several parts or particles of which an organism is composed. As far as structure is concerned, an elementary part of a fungus corresponds to an elementary part of one of the higher tissues. The germinal matter of each is capable of growing infinitely and may be divided into numerous smaller particles, each one of which is capable of growth, but the conditions necessary for maintaining the vitality of the fungus are so simple that each particle will live although separated from its

neighbours and exposed, within certain limits, to variations of temperature, moisture, &c. The particles of the germinal matter of the elementary part from any tissue of one of the higher animals, will only live when in contact with the fluids of the body which produced it or those of another body of the same kind. It cannot exist independently for any length of time and if the conditions under which it is placed normally, be very slightly altered, it dies. Under no circumstances can it produce an independent organism. Neither a portion of germinal matter nor an entire elementary part of a tissue of one of the higher animals can be regarded as an independent structure. It is only a part of an individual whole. On the other hand, a very small portion, far too minute to be seen by the highest powers, of one of the simplest and lowest forms of existence is independent, may produce, though isolated, a structure similar to that from which it sprung and may be regarded as an individual. The higher organism is composed of an immense number of elementary parts which are dependent on each other and cannot exist separately. An elementary part of the simplest organism is composed of an immense number of minute particles every one of which may live and grow and produce its kind independently of its neighbours and of the stock from which it was derived.

It will be inferred that I hold that vital power is not generally diffused over tissues but is restricted to the particles of the germinal matter only. Often a very gradual transition may be traced from the particles of germinal matter to the formed material. It is not possible to define the exact point at which a particle ceases to possess the power of animating lifeless matter and acquires the properties of the formed material. The change is a gradual one. Probably for a certain period particles possess the power of growing rapidly, dividing and sub-dividing into multitudes of new ones. Next the power becomes more restricted. They may divide into two, and the process may continue in the resulting parts, but at length this ceases and the particles become converted into the material, the production of which is the end for which they lived and were produced. One might say therefore that the vital activity of the particles gradually becomes reduced as they recede from the centre at which they became animated. If the term life and vital activity be used, several degrees must be admitted. The particles seem to pass by almost insensible gradations from the highest point of vital activity to a state from which they pass uninterruptedly towards a comparatively quiescent condition which is followed by death and disinte-

gration. Changes in chemical composition as well as in physical properties are associated with the different phases of existence. During the life of the particles as germinal matter, the arrangement of the elements must be altered in such a manner that new combinations may take place while the change into formed material proceeds. It is probable that very many substances of definite composition are produced and undergo conversion into other compounds during these changes.

The most important points which I have endeavoured to prove in this course of lectures may be summed up as follows.

1. That the smallest living elementary part of every living structure is composed of matter in two states, *forming* and *capable of increase,* upon which the active phenomena are entirely dependent,—and a substance external to this, which existed at an earlier period in the first state, but which is now *formed,* and destitute of the powers above referred to.

2. That the only part of a living structure which possesses the power of selecting pabulum and transforming this into various substances of growth, and of reproduction, is the active substance or *germinal matter.*

3. That the germinal matter possesses the power of growing infinitely but that it always grows under certain restrictions. The rapidity of its growth or extension is determined by certain conditions.

4. In all living beings the matter upon which *existence* depends is the germinal matter, and in all living structures the germinal matter possesses the *same general characters* although its *powers* and the *results of its life* are so very different.

5. An increase in the *number* of elementary parts always results from the division and subdivision of the masses of germinal matter. In many cases portions project some distance from the general mass and then become detached.

6. A mass of germinal matter which is endowed with powers different to those of the germinal matter from which it was derived, always originates as a new centre (nucleus or nucleolus) in pre-existing germinal matter. The origin of new centres is from within centres, or endogenously, but the mass of germinal matter which results multiplies by division.

7. During the life of every elementary part, a movement of the particles of the germinal matter takes place in a definite direction, from centre to circumference, and it is probable that by this movement of the particles *from* centres, the transmission of the nutrient substances in the opposite direction is ensured.

8. The relative proportions of germinal matter and formed

material vary greatly in different elementary parts, in the same elementary part at different periods of its growth, and in the same tissue under different circumstances. The more rapidly growth proceeds, the larger the absolute amount of germinal matter produced in proportion to the formed material. Rapidly growing structures are *soft* and *easily disintegrated*. Firm dense tissues are of slow growth, and the hardened *formed material* of which they mainly consist, resists disintegration and change.

9. The pus-corpuscle is a mass of germinal matter in direct descent from the germinal matter of an elementary part. The conditions under which the growth of the germinal matter has taken place have been such as to cause its rapid increase, and to interfere with the production of formed material. For some time before perfect pus-corpuscles were produced, a tendency to the production of elementary parts, like those of the original texture, was manifested.

10. The cell-wall is not a constant structure. The definitions generally given of the cell are not applicable to the elementary parts of many tissues. Pabulum does not pass through the cell-wall to become altered by the action of the cell, but certain of its constituents are converted into germinal matter,—the living substance which becomes tissue or is changed into substances which form the constituents of secretions.

11. In the nutrition of an elementary part the following phenomena probably occur. 1. Inanimate pabulum passes through the formed material into the central portion of the spherical masses of germinal matter, while, 2. Particles previously animated move outwards. 3. The outermost particles of the germinal matter become converted into formed material. 4. A corresponding quantity of the oldest formed material is disintegrated, or the new formed material is added to that previously existing, in which case this structure increases in quantity. In *nutrition*, without growth, an amount of inanimate matter becomes living germinal matter within a given time, exactly corresponding to the proportion of germinal matter which undergoes conversion into formed material, and this makes up exactly for the quantity of old formed material, which being no longer fit for work, is disintegrated, converted into soluble substances, and removed.

Connective Tissues.

12. The connective tissues as a class cannot, by any structural characters, be separated from other tissues of the body.

13. The chief differences between a structure like epithelium (cell tissue) and cartilage or tendon (connective tissue) are these. In the first, the formed material of each elementary part is more or less separated from that of its neighbours, while in the latter the formed material is continuous throughout, but in both cases, the oldest portion of the formed material is that which is farthest from, and the youngest, that which is nearest to, each mass of germinal matter.

14. White fibrous tissue and cartilage do not consist of *cells*, and an *intercellular substance* which is produced independently of cells; but the so-called intercellular substance exactly corresponds to the cell wall of an epithelial cell, and, like this, was produced from the masses of germinal matter (cells). No 'intercellular substance' is produced independently of the living active granular substance in the 'cell,' or *germinal matter*.

15. The 'nuclei' or masses of germinal matter of tendon correspond to the 'nuclei' of an epithelial cell. The fibres of yellow elastic tissue in tendon are neither connected with, nor formed from or by, these 'nuclei.' The matter of the 'nuclei' gradually undergoes conversion into the white fibrous tissue, while new nucleus or germinal matter is produced from the pabulum.

16. The 'mucous tissue' of the umbilical cord is a modification of fibrous tissue. No system of communicating tubes for the circulation of nutrient juices can be demonstrated in it.

17. In certain tissues (cartilage, epithelium) the masses of germinal matter produced by division are quite separate and distinct from each other, while in others (tissue of umbilical cord, tendon, periosteum, &c.) they remain for some time connected together. Thus a thread-like or stellate arrangement may be produced, and as the several masses become further separated, the points of communication are reduced to narrow lines and often disappear altogether.

18. The osseous tissue is composed of formed material which is afterwards impregnated with calcareous matter, and corresponds to the matrix of cartilage and to the wall of an 'epithelial cell,' as for instance that of a 'cell' of cuticle.

19. The lacunæ of living bone are occupied with germinal matter (nucleus) and formed material, in which calcareous particles are still being deposited from without inwards.

20. The canaliculi are mere spaces which are left during the accumulation of calcareous matter in the formed material. Through these channels fluids pass to and from the germinal

matter in the lacunæ. They are not *processes which grow,* but are merely *channels which are left.*

21. No dentinal '*tubes*' exist in living dentine. The 'dentinal tube' like the lacuna, contains germinal matter and formed material, and the latter is gradually impregnated with calcareous matter from without inwards,—that is, the oldest formed material first undergoes the process of calcification.

22. The so-called gray or gelatinous fibres are real nerve fibres, and there are many ganglia which are connected with these fibres alone. The ultimate ramifications of all nerve fibres closely resemble the gray or gelatinous fibres. These fibres are numerous in the pericardium and are distributed to all the vessels.

23. Certain forms of connective tissue may result from changes taking place in nerves and vessels. The modification of connective tissue met with in the papillæ of taste and touch, is probably, in great part, the remains of nervous structure which is incapable of being removed by absorption. Certain forms of connective tissue are produced by germinal matter but some varieties consist of the remains of structures which were active at an earlier period of life.

24. In some situations in which 'areolar tissue corpuscles' are said to exist, and to form a *special system of tubes and cells* connected with the *distribution of nutrient juices,* the following bodies may be recognized; nuclei of *nerves,* nuclei of *capillaries,* nuclei of *white fibrous tissue,* nuclei of *yellow fibrous tissue,* nuclei of *fat cells, lymph,* and *white blood-corpuscles.* Each of these masses of germinal matter is connected with the production of its own peculiar tissue or formed material, and there are no cells and tubes to be demonstrated which are concerned in the distribution of nutrient matter to these textures. The nutrient fluid permeates the tissue generally, and each mass of germinal matter selects its proper pabulum and undergoes increase, while the older particles undergo conversion into tissue.

ON THE SOLVENT POWER OF STRONG AND WEAK SOLUTIONS OF THE ALKALINE CARBONATES ON URIC ACID CALCULI.*

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Abstract.

THE design of the author was to show the fallacy of certain experiments that had been made on the solubility of uric acid calculi in solution of the alkaline carbonates; and to furnish some exact data from which to estimate the rate at which it is possible to effect solution of these calculi by alkaline carbonates.

About twenty years ago, the French Academy appointed a Commission, composed of MM. Gay-Lussac and Pelouze, to inquire and report on a number of conflicting communications that had been made to it by the advocates of solvents for urinary calculi and their opponents.

This Commission reported, in 1842, to the following effect. They had exposed numerous urinary calculi for a whole year to the contact of solutions of the alkaline carbonates, containing from 273 to 546 grains to the pint. None of the calculi were dissolved; and some were not diminished in bulk. Their loss of weight varied from a quarter to one-half.

In another experiment they passed, in the course of three months, 110 gallons of a solution containing a twentieth of its weight of carb. soda, over a number of fragments placed at the bottom of a glass funnel. The bulk of most of these was not diminished, and their loss of weight varied from 10 to 60 per cent.

They then tried experiments on the living body, by passing currents of the solvent through the bladder at blood heat by the double catheter. Here is a sample of their results. A patient who had been subjected to lithotrity, and whose stone

* This is the abstract of a paper read at the Meeting of the British Association for the Advancement of Science held in Manchester, 1861.

was known to be uric acid, had, at different times, 55 gallons of a solution of carb. soda, containing 130 grains to the pint, passed over a large remaining fragment, which had been carefully measured. This enormous mass of liquid produced no diminution in the bulk of the fragment; its only effect was to soften the surface.*

The conclusions of this report were wholly adverse to the advocates of solution; and they were formally adopted by the Academy.

The experiments, however, have a defect: the solutions used were too concentrated, and this circumstance vitiates the whole inquiry. The author found that very weak solutions of the alkaline carbonates dissolved uric acid calculi with considerable rapidity, while stronger ones altogether failed. In order to decide what strength of solution had the most solvent power, fragments of uric acid, weighing from 40 to 112 grains were placed in 10 oz. phials, and solutions of carbonate of potash and soda of various strength were passed over them at blood heat. The experiments were continued day and night; and the daily flow of solvent varied from 6 to 15 pints.

Operating in this way, it was found that above a strength of 120 grains to the pint there was no dissolution; and even with 80 grains to the pint there was only a little; but solutions of 50 and 60 grains to the pint dissolved the fragments freely. The cause of this difference was found to lie in a coat or crust of white matter which invested the stone in the stronger solutions. At and above 120 grains to the pint this coat was dense and tough, and could not be wholly detached from the subjacent surface. With 80 grains to the pint, it was brittle and easily detached like a layer of whitewash. With 60 grains to the pint and under, either no crust formed at all and the stone dissolved clean with a water-worn appearance, or it was only represented by a few loose flakes, scattered here and there over the surface, and offering no impediment to dissolution. This coating or crust was found essentially to consist of bi-urate of potash or soda, and its formation depended on the fact that the alkaline bi-urates are almost insoluble in any but very weak solutions of the alkaline carbonates. In the strong solutions the bi-urate remains undissolved and encases the stone in an insoluble investment; while in weaker ones it is dissolved as fast as it is formed, the surface of the stone remains clean, and dissolution proceeds without impediment.

The following tables are the results of forty-eight day experiments:—

* Comptes Rendus, 1842, p. 429.

TABLE I.—*Uric Acid and Carbonate of Soda.* (*Sod. Carb. exsiccat of the shops.*)

Strength of Solution.	Flow per 24 hours.	No. of Obs.	Daily average Loss of Weight per Cent.	Remarks.
Grs. per pint.	Pints.			
240	6	2	0	Covered with a dense coating of bi-urate.
120	6	2	0	Covered with a dense white coat.
60	14	2	14·3	Covered with a looser white crust, which was removed before weighing.
30	15	4	10·9	
30	8	2	10·2 } 10·3	Dissolved clean.
30	5	2	9·8	

TABLE II.—*Uric Acid and Carbonate of Potash.*

Strength of Solution.	Flow per 24 hours.	No. of Obs.	Daily average Loss of Weight per Cent.	Remarks.
Grs. per pint.	Pints.			
240	6	1	0	Covered with a tenacious white coat as if of paint.
120	6	3	0	Covered with a less dense coating. After detaching this and wiping, there was a mean loss of weight of 7·1 per cent.
80	6	2	9·8	Covered with a loose detachable white crust.
60	14	2	19·0 .. 20·2	Surface clean.
60	6	5	21·4 ..	Loose flakes in spots.
40	6	3	15·6	Sometimes a few loose flakes where the fragment rested.
30	15	4	13·0	
30	8	2	15·0	
30	4	2	9·5 } 11 9	Dissolved clean; occasionally a few loose flakes.
30	6	4	10·2	
20	6	3	11 0	Dissolved clean.
10	6	3	6·5	Ditto.

ON DIABETES INSIPIDUS.

By Peter Eade, M.D. (Lond.)
Physician to the Norfolk and Norwich Hospital, &c., &c.

IN Vol. II. of this journal I published a short paper on the subject of Diabetes Insipidus, in which a case of this disease was related, and some remarks were appended in reference to the probable nature of the disorder. I also there reported the principal *post mortem* appearances observed in another and fatal case that had fallen under my notice. Since that time two or three further examples of this affection have occurred in my practice, and as one of them has ended fatally whilst under my care, I desire now to record and call attention to the unusual condition of the kidneys, and supra-renal bodies discovered at the *post mortem* examination of the body.

The patient was a well-developed labouring man, aged about sixty-two, who was admitted into the Norfolk and Norwich Hospital, under my care, on August 31, 1861, suffering from great debility and exhaustion, apparently the result of the long continued discharge of very pale and copious urine. His history was, that for twenty years he had suffered much from thirst, and had been in the habit of drinking large quantities of fluid to satisfy this craving. He had, however, been in fair health until about two years ago, when his general powers began to fail, but he was not compelled to discontinue his employment until about nine months since.

During these nine months, in which he had been more particularly under observation, the quantity of urine discharged had often amounted to fourteen or sixteen pints daily, being always of very low specific purity, and had never contained either sugar or albumen. He had continued gradually to get thinner, weaker, and paler—the paleness being of a peculiar sallow tint, and sometimes amounting to actual duskiness. The thirst had been constant and often urgent, and the skin always dry and harsh. He had never suffered more than a very slight amount of pain in the back, and his feelings had generally been rather those of weariness and gradually increasing weakness, than of actual pain. His bowels were frequently much constipated, and when this was so, the stomach invariably rejected his food.

For a time he derived considerable benefit from a prolonged course of tincture of steel, but for the two or three weeks prior

to admission, the stomach had been excessively irritable, and he had suffered much from frequent vomiting, and its continued inability to retain its contents. This symptom had been somewhat relieved by the use of hydrocyanic acid and effervescing soda draughts, but had not quite ceased.

The day after his admission to the hospital, his bladder became unable to expel its contents, and from this time until his death, the catheter required to be used daily. The quantity of urine withdrawn was never less than from four to six pints in each twenty-four hours, and it was always pale, clear, acid, of specific gravity about 1005. He now became rapidly typhoid, the tongue and lips dry and brown, the pulse weak and failing, the stomach rejected nearly all nourishment, the complexion assumed a remarkably dirty yellow hue, and he died on September 8th.

Sectio Cadaveris, thirty hours after death.—Body somewhat emaciated; skin with a pale yellow, or sallow tinge.

Chest.—Lungs and heart healthy, but the latter organ rather large.

Abdomen.—Liver congested, especially in its centre, where it was soft in texture, and filled with black blood, almost to a state of parenchymatous apoplexy.

Spleen small, and bloodless, but healthy looking.

Kidneys.—Both organs diminished in size, deeply lobed on the surface, and very dense to the feel in the position of the cones. On section they were seen to be greatly wasted. The cortical portions very thin, and scarcely to be distinguished from the pyramidal. The cones were nearly absent, or rather were converted into dense fibrous tissues, containing many large cystiform spaces. The mucous membrane of the pelvis was thickened, fibrous-looking, and darkly congested. The pelvic cavities considerably enlarged. The right was, on the whole, rather more diseased than the left. Ureters a little dilated.

Bladder considerably enlarged. Its walls thin and pale, some blood effused under its mucous membrane. The vesical orifice of prostatic urethra large and evidently dilated.

Supra-renal bodies greatly diseased; both converted into flaccid cysts, capable of containing each some half ounce of fluid, with thin walls having a bile-coloured granular appearance. The left slightly larger than the right.

On microscopical examination the cortical portion of the kidneys was found to be firmer than in health. Many of the tubes very narrow, and much wasted, while others were twice the diameter of the healthy uriniferous tubes. The walls of the tubes were firm and thick. The capillary vessels every-

where contained numerous nuclei in their walls, and external to them was a considerable quantity of fibrous material, with very numerous nuclei. The Malpighian bodies were for the most part smaller than in health. The epithelial cells were also smaller, as well as more numerous, than in health, and the tubes appeared to be distended in many places by their accumulation.*

The general outline of this case of diabetes insipidus is not very dissimilar to that of many others which are on record, and especially agrees with some which are related by Dr. Willis. We have the usual sequence of great thirst, an excessive quantity of fluid drunk to gratify this craving, a consequent abundant flow of limpid urine; then, after a varying interval, signs of failure of nervous power, with loss of appetite, irritability of stomach, and a gradually increasing languor, and sense of debility.

The chief symptoms present in three cases, of which I have accurate notes, are shown in the following :—

Table of Cases.

H. L.	H. M.	H. R.
Age ; sixty-five years.	Age ; forty years.	Age ; sixty-two years.
Previous diseases; jaundice, chronic rheumatism, dental neuralgia, epistaxis.	Sub-acute rheumatism, bleeding piles, hœmoptysis.	Not known.
Urine copious, pale, clear, of low specific gravity, free from sugar or albumen.	The same.	The same.
Micturation frequent.	The same.	The same.
Micturation followed by uneasiness in glans penis.		
Weak pulse.	Pulse weak and slow, and heart's sounds very feeble, and often scarcely audible.	
Marked debility, and increasing feebleness.	Marked feebleness.	Increasing feebleness restlessness, and irritability.
Great thirst, gratified by drinking large quantities of fluid.	The same.	The same.
Slight emaciation.	The same.	The same.
Loss of appetite.	The same.	
Some indigestion.		

* This description of the microscopical appearances of the kidneys was kindly made for me by Dr. Beale, who adds, "That this multiplication of cells within the tubes, probably took place within a short period of death."

Table of Cases—Continued.

H. L.	H. M.	H. R.
Recurring diarrhœa.	The same.	No diarrhœa, but frequently constipation, and then always vomiting of food.
Pallor, a peculiar whiteness of complexion.	Pale and pasty complexion.	Pallor, becoming sallowness towards the close; skin dry and harsh.
Slight pain over sacrum, and in iliac regions.	Vague pains in the abdomen and limbs.	Slight pain in the back.
In latter period of life, very troublesome sickness.		The same.
Retention of urine preceding death.		The same.
Death by exhaustion.	Still alive.	Death by exhaustion.

The condition of kidney which is so markedly seen in this case (*vide* Plate X, fig. 1), and which is evidently one of inflammatory condensation and atrophy, existed, though in a lesser degree, in the patient whose *post-mortem* appearances are recorded in my former paper on this subject. Indeed, the kidneys altogether may be considered to be in the same pathological condition, although the longer duration of the disorder, and, perhaps, its greater intensity in the one case than in the other, had carried those changes to a greater extent. In both cases, the kidneys, previous to section, showed deep depressions on their surface, tending to divide the organ into separate portions or lobes, whilst the pyramids were very firm and dense, and yielded, when compressed by the fingers, a sensation as of small tumours or nodules. In both, division showed that a gradual destruction of the cortical portion was going on, with a simultaneous deposition of (or conversion of renal tissue into) fibrous tissue; and in both the pelves and ureters were dilated.

It is, perhaps, worthy of passing notice, that in another disease attended with a certain amount of diuresis, viz., chronic desquamative nephritis, there is also a tendency to a wasting and atrophy of the kidney; the organ being in these cases found after death to have suffered a diminution both of bulk and weight. But although this is so, it would, I think, scarcely be either safe or justifiable to draw from this fact any conclusion as to the dependence of the chronic diuresis upon any irritative or inflammatory condition of the kidney; for, on the one hand, we have an equal amount of diuresis in diabetes mellitus, where no such pathological condition is found, and on the other, there is no doubt that such inflammatory atrophy may be due simply

to the overworked and irritated condition in which these glands have so long been kept,—a condition which, though in all probability producing at first nothing more than passive congestion or an attempt at hypertrophy, would inevitably by degrees lead to condensation and degeneration of the excreting structures, even were there an absence of the destructive and sacculating influence upon the kidney which the constantly distended state of the ureters and pelvic cavities must be incessantly exerting.

This atrophied condition of kidney is well described by Rokitansky, who says,—"Chronic inflammation is, like the acute form, frequently followed by atrophy of the kidney, inasmuch as not only its product, but the original tissues themselves become absorbed. This secondary atrophy attacks either the entire kidney or sections of the organ; and the consequence is, accordingly, a uniform reduction of its size, or a partial contraction, which gives the kidney a shrivelled and uneven lobulated surface . . . . . On closer examination, we find the cortical substance (in extreme cases) reduced to a mere vestige; the pyramids are diminished to a size corresponding to the dimensions of the organ; the tissue generally is of a pale-red, or here and there of a slate-gray colour, denser, tough, and fibro-cellular."

If, then, this degenerated condition of kidney, marked and striking as it is, is only a secondary and not the primary disease, we are still as much as ever in want of an explanation of the real nature of the cause in operation to produce the diuresis and its secondary effects upon the kidney. I am not aware that the condition of the supra-renal bodies in this disease has ever been made the subject of observation, but I now wish to call attention to the fact, that, besides the disease of the kidneys, there was, in the case now reported, marked disease of both of these capsules,—a disease which was evidently of long standing, was apparently of a degenerative character, and which had resulted in a great enlargement of these organs, and their conversion into semi-pulpy flaccid cysts. Their natural function was therefore destroyed, and I would venture upon the suggestion of the *possibility* of some irritative disease of the supra-renal bodies being the exciting cause of the disorder known by the various names of Diabetes Insipidus, Hydruria, or Chronic Diuresis.

The great class of cases in which supra-renal disease was found to co-exist with a peculiar deposit of pigment in the skin and other tissues, to which Dr. Addison directed attention, has, (he says), for their leading features, anæmia, general languor, and debility, remarkable feebleness of the heart's action, and irritability of the stomach. In these cases also, we have all the

marked anæmia, increasing languor and debility, irritability of stomach, &c., upon which he laid so much stress, with the addition of diuresis. The dark discolouration of skin is, indeed, absent, but (merely noticing the fact that duskiness of the skin has not been present in all the recorded cases of supra-renal disease), I would observe that there is in its place a very evident alteration of colour, consisting in a loss instead of an addition of pigment, and a *whiteness* of complexion which has struck my eye as having a peculiarity quite distinct from that of chlorotic or ordinarily anæmiated patients. In Dr. Addison's cases, and, indeed, in nearly all those yet recorded, the disease was such as mechanically to interfere with the action of the supra-renal bodies, or to destroy them by acute inflammation. In my case the disease was probably of an irritative or chronically degenerative nature. The office of these organs is quite unknown; they are very largely supplied with blood-vessels and nerves; they are in immediate juxta-position with the kidneys. If they have any power of presiding over and regulating the complicated function of renal secretion (and may not this be a portion, at least, of their uses?), any continued irritation of their structure would be the very thing to induce such an exalted action of the kidney as would lead to an increased production of the peculiar elements which it was its special duty to eliminate, and one of which is undoubtedly water. That in those cases in which marked disease has been found in these organs, no diuresis existed, does not, in my opinion, annihilate this hypothesis, seeing that such disease may have been of an entirely different character from the one under consideration.

If, on further investigation, any connexion should be found to exist, as now suggested, between Diabetes Insipidus and disease of the supra-renal capsules, such a name as *Hydruria suprarenalis* might appropriately express the morbid condition. I am well aware how dangerous it is to attempt to generalize from a single case, or to lay too much stress upon pathological appearances which may prove to be merely coincidences, but in the case of the disease under consideration, I am so satisfied that we have something more to deal with than a mere habit of thirst, or a depraved condition of digestive or pharyngeal mucous membrane, at the same time that we are in such utter ignorance of what the morbid change may be that gives rise to the symptoms, that I feel no hesitation in venturing thus to throw out the suggestions I have now made, in the hope at least that they may lead others to examine into the condition of these much-neglected organs in this disease whenever the somewhat rare opportunity for so doing offers itself.

Part III.

RESULTS OF CHEMICAL AND MICROSCOPICAL EXAMINATION OF VARIOUS SPECIMENS.

LARVÆ OF CERTAIN SPECIES OF BLOWFLY EXPELLED ALIVE FROM THE BOWELS.

Dr. Brinton's Case in which the Larva of *Musca Sarcophaga* was found alive in fæces.

[*Extract from a letter to the Editor.*]

"I LATELY inspected the alvine evacuation of a patient immediately after its expulsion; and, noticing deep in the interstices of two of its triple colic rows of *scybalæ* what seemed to a casual glance an ordinary *oxyurus vermicularis,* I at once secured the specimen for some researches I have long been pursuing on the metamorphoses of this parasite."

"It was not till the next day that I had any further opportunity of examining the specimen, which had meantime been securely placed in a saucer moistened with distilled water, and covered with a bell glass. The moment I laid hold of it with the forceps, its smooth buxom skin, quite unlike the hard chitinous feel of the *oxyurus,* apprized me of my mistake in supposing it to be the creature I was in quest of; and to my amazement, in a few seconds, I was further disillusioned by the little creature lifting its head, and turning it round with that air of bland inquiry and expostulation with which a maggot seems to resent being thrown out of his bed and board to starve in a desolate world."

"The microscope confirms the evidence afforded by the appearance and manners of the creature. You will see that it is the larva of an insect, with branching trachcæ, numerous segments to its body, &c., &c. I only add, that the patient had

had no symptoms whatever referrible to the stomach or bowels, and has not detected any more *larvæ* in his evacuations since; and that the larva, to all appearance in a state of suspended animation when first noticed by me in the scybalous excrement, and recovering its vigour by a few hours exposure to the air, retained signs of life for more than thirty-six hours after its immersion in distilled water."

Its species I dare not decide; but it is evidently one of the *Muscidæ*, and not, I think, the *vomitoria*, but the *sarcophaga*, infesting cheese and bacon, to its involvement in which, it owes its occasional introduction into the human body. Counting the head as four small segments, I make out fourteen in all."

Case by Michael Blood, M.R.C.S. (St. Heliers, Jersey).

Mr. M., aged 39, applied to me eighteen months since, for great uneasiness in the rectum; a creeping, crawling sensation, attended with a sensation of sickness: his general health was good, save some slight gouty spmptoms occasionally. I directed a purge, with an injunction to observe closely the excretion, and he observed several of those nondescripts alive in the fæces; he picked out several and brought them to me in a bottle, they were in various states of development, and not having seen any thing like them before, I showed them to a *confrère* who had a microscope, who could not enlighten me on their kind or origin. I questioned Mr. M. as to the digesta he indulged in, and I found he had a partiality for German sausages, which he ate for breakfast frequently, and I told him I believed he took the cause in his sausage. He relinquished the use of the German sausage, but has had frequent returns of the annoyance. The last specimens I sent were followed by others similar since; purgation and various vermifuge medicines were had recourse to, with occasional cessation of the appearance of these creatures. But still in various shapes, gravamens, &c., they make their appearance; a very guarded diet is now to be adopted, and pork, cheese, and sausages, in every shape, are to be relinquished.

[The bodies alluded to were forwarded to me for examination by my friend Dr. Graily Hewett, and were of the same nature as those described in Dr. Brinton's case. Another example in which they occurred is referred to in the "Microscope in Practical Medicine," second edition, page 7.—*Editor.*]

CAST OF THE ŒSOPHAGUS COMPOSED ENTIRELY OF EPITHELIUM.

Forwarded for examination by S. Wood, Esq. (Shrewsbury).

The following is an extract from Mr. Wood's note:—"I feel induced to trouble you with the enclosed, although I know so little about it. It was given to me by a medical friend in Shrewsbury; all I know is, that a lady patient of his was for a long time troubled with sickness, which nothing would allay, and was reduced to extremities, when she vomited several pieces like the enclosed, but much longer, three inches in length. They appear membranous, but are not, I believe, of a vegetable nature; on being burned, they give out the peculiar smell of animal tissue. I have never seen anything like this; the thicker portion feels like the membrane of diptherite, but the thin, firm membrane is very peculiar. Is it an exudation from the œsophagus? I have just received another portion, seven inches long, which appears to be a cast of the œsophagus, and when fresh, was of a light skin colour."

Upon microscopical examination, it was found that Mr. Wood's conclusion, as to the nature of these membranous masses was quite correct; they were composed of the firm and closely matted layers of squamous epithelium, which forms the lining of the œsophagus; several of the masses formed complete tubes. The case is especially interesting, as demonstrating the fact that a considerable thickness of an epithelial layer may be removed from many surfaces. Cases are recorded in the "Archives," in which large plates were removed from the mucous membrane of the stomach, small intestines, uterus, and vagina, and below an example of the same change, affecting the epithelial coat of the large bowel of a child, is given.—[L.S.B.]

CASTS CONSISTING OF FLAKES OF EPITHELIUM AND MUCUS PASSED IN THE STOOL BY A CHILD AGED FOUR YEARS.

Sent for examination by James Borrett, M.D. (Sherborne).

The masses were tolerably firm, and some of them were evidently portions of a tube. They were passed by a child, aged four, without giving rise to any urgent symptoms. On microscopical examination, the tissue was found to be composed of a very firm mucus, in which numerous cells of epithelium from the large intestines, were imbedded. The following notes of the case are extracted from Dr. Borrett's note.

"The casts of mucus and epithelium were passed by a little girl after some weeks of pain in the body. My fears were that some foreign body had been swallowed; a button having

once been passed up the nostril, and not recovered. We always had a difficulty in getting the little girl to sit down, and relief of bowels always caused more or less pain."

"The substance came away after a strong dose of senna tea, which produced great griping; it had been found that senna always caused distress, and castor oil was the aperient used afterwards. There was increased sensibility of the canal, which made senna a bad aperient."

"The mucus and epithelium cast of bowels was passed in February, 1860; since which time, the child has enjoyed good health; she never makes any complaint of pain in the bowels; the appetite is large, and the general condition of the child excellent."

DIPTHERIA IN THE PIG.

Some time since, my friend, Mr. McCormick, of Aylesbury, sent me for examination, the tongue and part of the pharynx of a pig, covered with a very thick, false membrane. The layer, on the posterior part of the tongue, was of a finer consistence, and about the eight of an inch in thickness. It consisted of a firm material, which was fibrillated, numerous small granular cells, about the size of white blood corpuscles, and epithelial cells, of various ages. From its deep surface, small funnel-shaped processes projected to the distance of a quarter of an inch into the follicles in the mucous membrane, at the lower part of which the multiplication of the granular corpuscles was taking place, apparently with great rapidity. It is probable that had the animal lived, the condition above described, would have soon given place to the process of suppuration, in which case, the mucous membrane in its entire thickness, must have been destroyed.—[L.S.B.]

CASTS OF THE SEMINAL TUBULES.

I have sketched very roughly in plate XIII, of the "Illustrations of Urinary Deposits," the character of some casts, which I believed had been formed in the seminal tubules. I have since seen several specimens of the same character, and in some a few spermatozoa were entangled; but a few days ago, very perfect casts of this kind were found in the urine of an old man, nearly 70 years of age. Amongst the long transparent casts, were others containing numerous spermatozoa. As to the origin of these latter, therefore, there can be no doubt whatever. In Plate X, fig. 4, I have represented one of these casts, containing spermatozoa, and some of the transparent mucous-like casts which, I believe, have also been formed in the seminal tubules.—[L.S.B.]

Part IV.

INSTRUMENTS AND APPARATUS OF PRACTICAL VALUE IN CARRYING OUT SCIENTIFIC INQUIRIES BEARING UPON MEDICINE.

COMPRESSORIUM FOR PRESSING DOWN THE THIN GLASS COVER WHILE CEMENTS OR CANADA BALSAM ARE DRYING.

By F. P. Hoblyn, F.R.C.S., Bath.

And improved by Dr. Falconer, of Bath.

Plate X, Fig. 4.

THE body is composed of a framework of mahogany, 12 inches in length, 3 in width, and 3 inches in height. (Plate XI, fig. 6.)

Nine mahogany fingers, 6 inches in length, are seen passing through holes in the top of the framework, and through corresponding holes in a thin support, to give steadiness to the fingers, so that they may move up and down without any lateral motion.

A round elastic passes through holes made very smooth in the upper part of the fingers, and through small brass eyes attached to the upper surface. This is fastened at the side. The elastic, with hardly any friction, acts as an efficient spring on the fingers; and, by the two hooks, it may be tightened or slackened at pleasure. This part of the arrangement, by which the power of the spring can be altered, was the suggestion of Dr. Falconer.

The apparatus may be French-polished; but it must be borne in mind that the polish will adhere to any slides which may be put on hot; a thin piece of wood, or an extra slide should therefore be placed underneath.

Both sides of the apparatus are of course open, and there is sufficient room for nine slides to be pressed at the same time.

ON DEMONSTRATING MICROSCOPICAL SPECIMENS TO LARGE CLASSES OF STUDENTS.

By Lionel S. Beale, M.B., F.R.S., F.R.C.P.,

Professor of Physiology in King's College, London. Physician to the Hospital, &c.

In the present day, every one who is following out any special line of investigation desires not only to add to the existing knowledge, but feels a wish to place the means of demonstrating the phenomena he has observed at the disposal of others. Facilities for demonstrating facts at present known are scarcely second in importance to original investigation. Teachers of minute anatomy labour under great disadvantage in not being able to demonstrate to their class the various structures they describe. A good preparation well shown will teach a student more, and, at the same time, give him more accurate views of the nature of the structure than the most carefully drawn diagrams, or the most graphic description. In various branches of medicine demonstrative teaching is of the utmost importance; and it seems to me that when actual specimens are appealed to during an oral lecture, and at the same time reference is made to well-executed plans of structure and drawings from nature, the difficulties of learning minute details are, in great part, removed. Real facts are imparted to the student, and he gains ideas of objects from the objects themselves; so that he is less likely to have to unlearn what he has already acquired.

For many years past I have tried various plans for demonstrating microscopical specimens to large classes of students, but, until quite recently, without success.

At the College of Surgeons, as is well known, a theatre has been expressly fitted up for demonstrating microscopical specimens. The plan adopted by Professor Quekett was to arrange a continuous flat surface, on which the microscopes, placed on stands provided with rollers, could be easily moved onwards. By having two rows thus arranged, more than fifty persons could see the specimens. It need hardly be said, that such an arrangement, however efficient it might be, was far too costly for general adoption. Although the movement was very smooth, the vibration while the microscopes were being moved was too great to permit of very high powers being employed;

and in order to show several specimens to many persons within an hour, it was necessary to be provided with several large, and, of course, very expensive instruments.

It was not possible for me to adopt such a plan as this; and I have tried a variety of expedients for effecting the same object in a more simple and less costly manner. The one I am about to describe has been fairly tried in several different classes, varying in number from 20 to 130, during the past twelvemonth. It has succeeded so well, that I feel sure it is suitable for general adoption, not only for scientific, but for elementary popular teaching, even in village schools. It is also inexpensive, and the arrangement is so simple that it cannot easily get out of order. The microscope used is the clinical pocket microscope described in page 289, Vol. II, and figured in Plate XVI. It is also described in the "Transactions of the Microscopical Society," Vol. IX, page 3. This instrument is placed in a small wooden stand, as shown in fig. 10, page 215 of the "Archives," Vol. II. To this an oil lamp is adapted, but the stand may be used by daylight in a room with a skylight by substituting a mirror for the lamp. I am in the habit of employing the instrument in this manner in my clinical demonstrations. It is unnecessary for me to describe the stand, which is of wood, as the drawing referred to above renders any detailed description unnecessary.

In Plate XI, fig. 5, is shown an arrangement, by which a diaphragm, condenser, mirror, polarizing apparatus, and other instruments, can be adapted to the pocket microscope. The different parts will be found fully described in the "explanation of the plates." The round stem on which these are made to slide, screws into the lower part of the stage by a screw almost as wide as the tube, and it may be firmly fixed in its place by a side screw, which presses on the neck just above the thread of the screw.

In fig. 3 is seen a very simple arrangement, by which four instruments are firmly fixed in a stand, which may be placed in front of a window so that direct light may be obtained, or lamps may be placed behind each specimen, or at the side when reflected light is required. The box in which these instruments are placed, is enclosed, above and at the back, by glass, so that the preparations cannot possibly be disarranged by any one. Any alteration in the focus is readily obtained by drawing the tube, in which the eye-piece is placed, up and down as before described. Specimens may be arranged thus and left for examination for hours, without any alteration whatever being made in their position.

Fig. 1 represents a modification of this arrangement, which I have found very useful for demonstrating delicate specimens to a large number of persons. Eight preparations arranged thus take up a very small space, and every one can walk round the apparatus, examining one specimen after the other. The lamp being placed in the centre, illuminates all the preparations. An ordinary French moderator lamp gives a good light, and it may be wound up from time to time by a long key. The entire apparatus is about sixteen inches high and 15 wide in its widest part. The arrangements for fixing the instruments are seen at a glance in fig. 2, and the position of the lamp is also shown. The description of each specimen is written on ground glasses, inserted in the cover, and these are lighted by the same central light.

The stage of the clinical microscope is a very convenient form for photographic purposes, and by adapting the tube to an ordinary camera a very simple arrangement for photographing microscopical preparations is readily made.

All the plans of demonstration I have described, are comparatively very inexpensive, and are adapted as well for popular demonstration, as for higher educational purposes. The focus is easily obtained, and with very little practice a person who had never had a microscope in his hands before, could arrange a preparation in one of these instruments, for demonstrating to a class. I believe that as this plan comes into more general use, each instrument, with its stand, will be made complete with powers, for about three pounds.

I am anxious that the objects I have had in view in arranging these instruments should not be misunderstood. They are not intended for microscope *work* generally, but merely for demonstrating objects to a number of persons. The instrument alone will be found useful as a pocket microscope for field work, but for preparing specimens and for general microscopical observation, the instrument is by no means convenient. Mr. Highley has lately made an arrangement by which the tube of an ordinary microscope may be detached and used as a pocket instrument; but, as a general rule, it will be found convenient to be provided with one of these instruments as well as an ordinary microscope. The apparatus I have described may now be obtained of Mr. Highley, 70, Dean-street; of Mr. Matthews, Portugal-street, Lincoln's-inn; and of other microscope makers.

Part V.

REPORTS OF RESEARCHES PUBLISHED ELSEWHERE.

REPORT ON MUSCULAR CONTRACTION,

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(abstract.)

UEBER DIREKTE UND INDIREKTE MUSKELREIZUNG MITTELST CHEMISCHER AGENTIEN. Von D. W. KUHNE. Müller's Archiv, 1859, p. 213.

UEBER MUSKELZUCKUNGEN OHNE BETHEILIGUNG DER NERVEN. *Ibid.* p. 314.

UEBER SOGENANNTE IDIOMUSKULARE CONTRACTION. *Ibid.* p. 418.

UNTERSUCHUNGEN UEBER BEWEGUNGEN UND VERANDERUNGEN DER CONTRACTILEN SUBSTANZEN. *Ibid.* pp. 564 and 748.

UEBER DIE CHEMISCHE REIZUNG DER MUSKELN UND NERVEN UND IHRE BEDEUTUNG FUR DIE IRRITABILITATSFRAGE. Muller's Archiv, 1860, p. 315.

UEBER DIE WIRKUNG DES AMERIKANISCHEN PFEILGIFTES. *Ibid.* p. 477.

FOR some years past the question of muscular irritability has been attracting an unusual share of attention among German physiologists. Indeed, since Bernard, in 1844, instituted his first experiments with the Woorari poison the discussion has been carried on with great intelligence and zeal. No one, perhaps, has contributed more facts, or has reasoned out the entire question more carefully than Dr. Kühne, of whose experiments and arguments we propose to give a brief abstract, confirming and contrasting them, as we proceed, from the observations of others of his countrymen, who have been simultaneously engaged in the same field. Although each paper is to a great extent independent, and it is obvious that, when writing the earliest of the series, the author scarcely anticipated the direction which his researches might ultimately take, we prefer analyzing them as a whole, selecting from each as occasion may require, inasmuch as one broad and definite idea evidently underlies the whole series,—that of establishing the intrinsic value of Haller's doctrine of muscular irritability.

We will then start with a statement of the author's observations on the mutual anatomical arrangement of muscle and

nerve. He thus describes it in the sartorius of the frog, the muscular and connective tissues of which he previously renders transparent by soaking it for twenty-four hours in hydrochloric acid of the strength of 0·1 per cent. The main nerve-trunk reaches the muscle at right angles to the direction of its fibres and at the lower portion of its middle third. It immediately divides into two branches, which tend to the opposite ends of the muscle. These primary branches divide and subdivide dichotomously, usually sending off a few recurrent twigs at each bifurcation. Microscopically, the primitive nerve-fibres will be found to subdivide. They run parallel to and between the muscular fasciculi, each breaking up into secondary tubes by bifurcation, often with the formation of distinct tertiary tubes by the splitting of the secondary ones. At a certain point, however, the nerve-tube will be observed totally to disappear. Occasionally a secondary fibre may at this point be seen apparently to unite with a muscular fasciculus, a slight nodular swelling indicating the point of junction. In the frog, however, Kühne was quite unable to trace the nerve through the sarcolemma. There are districts in every muscle in which the most careful examination fails to detect any trace of nerve. The upper wide end of the sartorius of the frog is entirely devoid of them in its terminal 2-5 millimetres, and none are to be detected in the lowest 1-3 millimetres of the muscle. Even in vertebrate animals it was possible to prove that the nerves were throughout provided with white substance. This never disappears, but the double contours are lost simultaneously. Meissner* was one of the earliest observers to trace the nervous structure beyond the sarcolemma. He describes the primitive fibres as being $\frac{1}{800}'''$ in diameter. They invariably run parallel to the muscular primitive fasciculi, but neither on the fibres nor on the primitive nerve-trunks could a neurilemma be distinguished. When the primitive nerve-fibre reaches the edge of a muscular fasciculus he states that it widens considerably, becomes triangular, and that its base so adheres to the margin of the muscle as to constitute a perfect union of these parts. Similar observations were made by Munk.† Kühne examined the muscles of the thigh of hydrophilus piceus and of oryctes nasicorins by means of polarized light, as proposed by Brücke, and in them he observed the nerves to pierce the sarcolemma, becoming simultaneously divested of their sheaths.

Our readers may recollect that Leydig‡ described a system

* Zeitschrift f., W. Zoologie, B. V. Anatomie und Physiol.. v. Mermis Albicans.

† Göttinger Nachrichten, J. 58.

‡ Lehrbuch d. Histologie, p. 135.

of cavities in muscle, under which he included all the so-called nuclei of muscle. Kölliker* considers all these to be real nuclei, but regards himself as the discoverer of true vacuoles, filled with a finely granular mass.† Kühne has seen large vesicular nuclei, fine linearly-disposed granules and vacuoles of various sizes devoid of granules. These last are usually spindle-shaped, and are sometimes seen to be united in groups of two and three by a canal. Slight pressure causes them all to vanish. Their red aspect separates them from the nuclei. The rows of fine granules are also to be found in every muscle in its entire length. Every primitive fasciculus in hydrophilus and oryctes, so long as it is irritable, shows one or more very regular tracts of large granules. One streak appears to run along the axis, and other two at the border, close under the sarcolemma, these occasionally anastomosing to constitute a fourth streak. They are distinguished by their finely granular or dusty aspect. These organs are in intimate relation with the nerve-fibres that break through the sarcolemma. Whenever the nerve pierces the sarcolemma it is where such a row of large granules courses along it. Only a short blunt extremity of the axis-cylinder is visible, and this appears to become granular and to identify itself with the substance lying between the large granules. Thus the rows of granules in the muscles of insects are but the extension of the true intra-muscular axis-cylinder of the motor nerve-fibres. The termination of this arrangement consists in the gradual dwindling away of the rows of granules till the eye can no longer discriminate between the ultimate ends and the contractile substance which is regularly traversed by the disdiaclasts.

Beale has shown that, of the oval nuclei seen in connection with the elementary muscular fibres of vertebrate animals, some belong to the capillaries, some to the nerves, and others are the nuclei of development of the contractile tissue. The last are always arranged longitudinally. The nuclei of the capillaries and nerves pass in different directions, *longitudinally*, *transversely*, and *obliquely*, always *on the surface of the fibre*. Beale describes every fibre as abundantly supplied with nerves, and states that the oval nuclei are the organs through which the nerve acts on the muscle. The nerves form a network on the surface of each fibre; and he has seen this in preparations of the mouse and other mammalia, in which the capillaries *had* been injected with Prussian blue fluid. No white substance or tubular membrane can be detected; but the delicate fibre can be seen in the intervals, between the nuclei, having a pale

* Gewebelehre, p. 180. † *Ibid.*, p. 174.

granular appearance in the preparations which have been preserved.* Beale believes that the granules and nuclei, which have been considered by some authors as elongated spaces, seen amongst the fibrillæ (especially in the frog), exactly correspond to the so-called nuclear fibres in tendon, and really consist of nuclei (masses of germinal matter) and imperfectly formed fibrillæ which are undergoing development.

Struck by the scantiness of our knowledge of the effects of different chemical substances as excitors of muscular action, according as they were applied to the motor nerve or to the muscular section respectively, Kühne instituted an elaborate series of experiments, in order to ascertain if, from the nature of the excitant, it were possible to demonstrate that the sarcous tissue were capable of direct excitation, *i.e.*, irrespectively of its motor nerve.

In all his experiments, unless it be expressly stated to the contrary, he employed the sartorius of the frog, which, from the length and great parallelism of its fibres, and from its nervous distribution, he considers to be peculiarly adapted for experiment. The following are the results which he obtained: —*Action of Acids.* Hydrochloric acid, if applied to the nerve trunk, required to be of a strength of 19–20 per cent. to induce contraction. On the other hand, an acid of the strength of 5, or even of 1 per mille, applied to the section of the sartorius, sufficed to induce contractions as active as those of the strong acid when applied to the nerve. Nitric acid only acted through the nerve when of a strength above 15 per cent., but a solution of 5 per mille applied to the muscular section proved abundantly efficient. Sulphuric acid he avoided, as it is impossible to discriminate its immediate effects from the results of thermic irritation. All these acids he presumes to affect the arcous substance by dissolving the syntonin, and not simply by altering the reaction of the section. Chromic acid applied to the nerve required to have a percentage of 5 parts to induce contraction, whereas a dilution of 5 per mille acted powerfully on the muscular section. Concentrated acetic acid, with equal parts of water, acted when applied to the nerve, whilst an acid of 6 per cent. dilution distinctly affected the muscular section. The same held of phosphoric acid.

Action of Alkalis.—The contrast of the direct and mediate effects of these bodies was far less decided than in the case of the acids. Thus of caustic potash Kühne says that a dilution of ·8 per cent. constantly caused contraction when applied to the nerve, and that even ·1 per cent. was not unfrequently

* Phil. Trans. Royal Society, 1860.

efficient, whereas, when applied to the muscular section, ·2 or even ·3 per cent. gave very uncertain results. Caustic soda acted similarly. If an entire sartorius were dipped into a solution of ·1 per cent., it contracted tetanically, and at once lost all irritability, even to the strongest streams of the Du Bois Regmond's induction apparatus. The action of ammonia proved to be very remarkable. As soon as its vapour became perceptible to the smell, the muscle began to contract, and as the rod is approached to the section a true tetanus ensued. The sensibility was so extreme that the minimum percentage of the solution could not be determined. If the muscle, however, were so sealed away that the nerve only could be exposed to the vapour or to the solution, no contraction whatever followed, however strong were the solution employed. The nerve can be exposed alone by drawing it through a hole in a piece of glass, and fastening it in with fat. He also employed lime solution, but of what strength the atmospheric air prevented him from determining. The nerve soon lost its irritability, whilst the muscular section long retained it. *Metallic salts.*—1. Sulphate of copper. Neither saturated, nor any other solution caused contraction when applied to the nerve, but all forms of concentration down to 4 per cent. caused violent contraction when applied to the muscular section. 2. Sulphate of iron had just the same effect on the nerve as the former. A solution containing 2–3 per cent. of the salt acted on the muscular section. 3. Sesquichloride of iron acted through the nerve if of a strength of 20–30 per cent., whereas a dilution of 1 per cent. acted amply on the muscular section. 4. Sulphate of zinc proved an excitant for the nerve down to 20 per cent., but to the muscle down to 1 per cent. 5. Chloride of zinc acted more forcibly through the nerve than any other metallic salt. Applied in a syrupy condition it scarcely affected the muscle, although if diluted it acted strongly, even 1 per cent. solutions were quite efficient. 6. The neutral acetate of lead in saturated solution only occasionally acted through the nerve. The minimum point for the muscular section was 4 per cent. 7. The basic acetate when of a strength above 10 per cent. acted through the nerve, but a strength of 2 per cent. sufficed to excite the muscular section. 8. Nitrate of mercury acted on both nerve and muscle. 9. The bichloride of mercury never excited the muscle indirectly, and its direct effects were somewhat irregular. 10. Nitrate of silver acted through the nerve. 11. Chloride of sodium is an active excitor both directly and indirectly, but it must be rather more concentrated for the latter. 12. Chloride of calcium only affected the nerve when

in strong solution, but the application of a fifty-fold dilution to the muscular section induced contraction.

Organic acids.—1. The action of oxalic acid was very uncertain. 2. Acetic acid must be concentrated to act through the nerve, whereas its vapour abundantly affected the muscular section. 3. When the end of the nerve was dipped into syrupy lactic acid, spasm at once set in, but when the muscular section was touched with the same, no result ensued, and it was only when the muscle was buried in the acid that it gradually drew itself together for a final rigor. Here, then, the usual conditions were reversed. But if the acid were diluted with equal parts of water, it ceased to work on the nerve, but acted with great power on the muscular section. Creosote and carbolic acid acted powerfully on the nerve, and but slightly on the muscular section. Concentrated alcohol also acted on the nerve, although in no degree of concentration did it affect the muscular section. Ether and chloroform applied to the nerve scarcely ever caused contractions, but the approach of an open bottle of the former to the muscular section induced gradual and permanent rigidity. If the muscle were left in a space saturated with the steam of warm water, it gradually recovered its irritability. Chloroform rapidly applied to the muscular section caused spasm. If the cut end of the nerve be dipped into pure glycerine, in a few seconds feeble fibrillar contractions are observed in the gastro-cnemius. These extend in the breadth of the muscle, until at last the entire limb passes into a tetanic state as complete as that produced by strychnia. But if the transverse section of a sartorius be dipped into glycerine, no spasm will result. If the muscle, however, be dipped into a dilution with 5 parts of water, it will contract every time a fresh section touches the fluid. If diluted with more than 2 parts of water, glycerine ceases to act on the nerve. Thus, the limits of its direct and indirect exciting powers are strictly defined. The earlier experiments with bile were very contradictory, but ultimately the following facts were elicited. Bile has a real exciting influence on both muscle and nerve. Many specimens of bile are not sufficiently concentrated to excite through the nerve trunk, but a little evaporation will render them efficient. Every specimen is sufficiently concentrated to excite from the muscular section. Even a dead and putrefying muscle if dipped into certain specimens of bile will undergo a peculiar steady kind of rigor, which must of course not be confounded with a true contraction. The biliary alkaloids have a similar action to the bile itself. A solution of 1 or 2 per cent. will affect the muscular section, but 6 per cent. of the salt is required to influence the motor nerve.

Conclusions.—As a rule, the muscle is more irritable than the nerve. The re-agents employed may be thus subdivided: 1. Those that affect the muscular section in a dilution greatly inferior to that in which they affect the nerve; of these hyhrochloric and nitric acids may be taken as types. 2. Those that act on muscle in a concentration in which they no longer influence the nerve, as chloride of sodium, chloride of calcium, acetic acid, lactic acid, glycerine and the biliary alkaloids; 3. Potash and soda affect the muscle and nerve about equally. A 4th class act violently on the muscle, and not at all on the nerve, as sulphate of copper, and particularly ammonia. A 5th series will excite through the nerve but scarcely by direct contact with the muscle, as creosote, alcohol, concentrated glycerine, syrupy lactic acid. A last class may be said not to affect either organ sensibly, as the fatty oils, and turpentine.

In perusing the results of this series of experiments one broad question starts to the mind. When we directly irritate the muscle by means of chemical re-agents, do we affect the contractile substance, or only the intermuscular nervous twigs? To determine this point, Ludwig demands that we should either succeed in obtaining contraction from a muscle which is destitute of nerves, or whose nerves have been functionally annihilated to their extreme ends.* This postulate was a few years ago believed to have found its answer in the researches of Bernard and Kölliker, into the action of Woorari poison; the former concluding that its effects were manifested on the peripheral motor nerve system,† the latter that urari poisons the motor nerves of the voluntary muscles through the blood, and in frogs destroys the muscular nerve termination in a few minutes."‡ To these statements, however, Schiff§ raised the serious objection, that all the observed phenomena could be explained by presuming those portions of nerve which are endowed with white substance to be alone affected. Funke also urged some difficulties in the way of the reception of Kölliker and Bernard's theory. (Beiträge zur Kenntniss d. Wirkung des Urari, etc. Verhand d., K. Sächs, Gesellchaft, 1859.) But its most decided antagonist proved to be Eckhard, who argued that inasmuch as the poison particularly affected the nervous system, it attacked the ganglia of the heart, and weakened the force of the heart's stroke, so as to retard the circulation in the muscles, and thus rendered it impossible for perfect paralysis of the ends of

* Physiol., 1 Aufl., Bd. I., p. 355.
† Leçons sur les effets des Substances Toxiques et Medicamenteuses.
‡ Virchow's Archiv. B.X., p. 71.
§ Physiol. Muskel Reizbarkeit, p. 19-20.

the motor nerves to occur within them; thus, the contractions obtained after Urari poisoning were to be referred to some residue of nerve force still left in the muscle.* He further argued, that when the motor nerves were paralysed to their physiological extremities, the muscle was quite incapable of responding to any stimulus whatever. The question can only be cleared up by a careful study of the effects of direct irritation on muscles poisoned with curari, and the objections would certainly lose force if any essential deviation from the standard could be noted in the form or character of the contractions. The idea that muscular irritability was actually increased in this form of poisoning was disproved by the following experiment by Rosenthal.† Two thighs being prepared according to Du Bois' method, so as to poison the gastro-cnemius of the one but not of the other, these muscles were so arranged as to be exposed to perfectly equal induction streams. The secondary spiral was then approached, and as the irritation increased contraction invariably began earlier in the unpoisoned than in the poisoned muscle. Kölliker, however, believes that in Urari poisoning the muscles evince a greater disposition to purely local‡ contractions.§ Haber also says, that "the muscles when brought into immediate contact with curari do not lose their capacity of responding to direct excitation, but the contractions are limited to those fasciculi to which the irritation is directly applied" (Müller's Archiv., 1859, p. 115). Kühne objects that the muscle employed by Kölliker (the Reichert's skin muscle of the frog) was not adapted to solve the point at issue, as it is impossible to procure it without injuring some of its longitudinal fibres. He also objects to the electrical test as employed by Kölliker, that in addition to the streams of greater density between the two electrodes, stream curves of lesser density traverse the whole muscle, so that a muscle in appearance only locally irritated may be excited throughout its whole extent. Employing the sartorius of the frog, he repeated these experiments, the electrodes being so arranged as only to expose a minute piece of the muscle to the stream, and the coils being very gradually approached, so that the secondary currents should be too feeble to be capable of any disturbing influence. He then observed that the portion of muscle which lay between

* Beiträge zur Anatomie, vol. I., p. 47.

† Uber die relative Stärke di direkten u indirekten Muskelreizung. Moleschott's Untersuchungen, vol. 3, 1857.

‡ The word local is used by Kölliker to signify either the contraction of a few fasciculi in the long axis of the muscle, or a contraction of a portion of the length of a fasciculus only. He here applies the term in the latter acceptation.

§ Op. cit. p. 133.

the plates never began to contract alone; but that as soon as the secondary spiral acquired a determinate relation to the primary coil, the whole muscle invariably contracted in its entire length. Had Kölliker's statement been correct, only the portion included between the electrodes should have contracted. Kühne then submitted muscles poisoned with curari to the series of chemical tests above referred to, with these results. Bodies that do not act on the healthy muscle are also inactive on the poisoned one. Solutions so dilute as just to cause twitching in the healthy muscle also excite the poisoned one. In short, all that has been said of direct muscular irritation holds, without exception, of the muscles of frogs poisoned with curari. Now no experiment is more adapted to bring forth Kölliker's local spasm than chemical irritation, yet it was never observed. The inference is, that the action of curari alone is incapable of deciding the question of muscular irritability. We shall subsequently return to the estimate of the actual value of curari.

We have just heard Eckhard talk of paralysis of the ultimate ends of motor nerves. The method by which he believed himself to have attained this desideratum was by the application of a constant electrical stream along the track of the motor nerve, the direction of the stream being from the muscle towards the nerve centres. Thus the positive pole was situated between the muscle and the negative pole. The nerve being exposed to this ascending current, he then tested the muscle itself with a second electrical apparatus, and ceased to obtain any contraction from its application. They at once re-appear when the paralysing chain is opened.* Pflüger deduces the law, "every constant stream which flows through any portion of a motor nerve diminishes the irritability of the same at all points on the side of the positive electrode, consequently if the stream ascend, the nerve will be less irritable than before, even to its extreme ends." † Now Kühne most reasonably objects to the employment of electricity as a direct muscular test when the nerve is thus exposed, and he urges the advantage to be derived from the use of chemical excitants. Still employing the sartorius and its nerve, he exposes the latter in a small gutta percha conduit to the action of the constant stream, allowing the muscle to hang free by its lower tendinous end. Every precaution being then taken to prevent dragging or desiccation of the parts, the muscle is tested by a direct electrical stimulus. The constant ascending stream is next opened on the nerve, and the muscle is thus brought to rest.

* Eckhard. Op. cit., p. 48. † Pflüger, Physiologie, d. Elektrotonus.

It will then be found requisite to advance the secondary spiral of the induction apparatus, which is being used as the medium for direct excitation, considerably, in order to cause the muscle to re-act. Similar results will ensue if a Grove's cell and Rheochord apparatus be employed as the measure of the intensity of the direct stimulation applied to the muscle. Moreover, the application of a metallic rod, or touching the muscular section with a non-exciting fluid, will not cause the slightest reaction. We are now in a position to apply chemical excitants to the muscle, whilst its nerve is thus paralyzed. If a vessel with dilute hydrochloric or nitric acid be approached to the muscular section, a single forcible contraction will ensue in the entire length of the fibres. A dilution of $\frac{1}{1000}$ of hydrochloric acid acted as strongly as in the series of experiments already detailed. The same holds of nitric acid. The actions of potash and soda were found identical with those already observed, and tetanus could be induced three or four consecutive times by the employment of the remarkable agent ammonia.

The results of experiments with chloride of sodium, sulphate of copper, chloride of calcium, dilute glycerine, etc., fully confirmed what has been already advanced. Thus the objection of Eckhard, that the loss of irritability by the ascending constant stream is not confined to the nerve, but passes into the muscle, is fully met. The muscle responds most decidedly to its appropriate stimuli when its nerve is in the state of anelectrotone. Eckhard has, however, objected to the use of chemical irritation at all. But Pflüger* shows that if a nerve be excited by such a substance as chloride of sodium, and the constant ascending stream be then applied, the tetanus induced by the chloride of sodium will be at once arrested. This experiment not only brings chemical and electrical tests into harmony, but demonstrates that the ascending stream paralyses the nerve at every point to which chemical irritation can be applied. Kühne, indeed, has shown that this law is applicable to the ultimate primitive fibres. In order that the ascending stream may neutralize a contraction, resulting from irritation of that mixture of muscle and nerve which is afforded by an ordinary section, it is necessary that the direct excitant employed should be capable of affecting one factor only of the combination, *i.e.*, the nerve. Such a substance he finds in concentrated glycerine, which we have seen to cause the most violent tetanus when applied to the nerve, but when applied to a section close to either extremity of the sartorius, to remain inoperative. If, however, a section be made nearer to the point of entrance of

* Physiologie, d. Elektrotonus.

the nerve, 5–6 millimetres from the end of the muscle, and the glycerine be then applied, after a time contractions will ensue. These are due to excitation of the intramuscular nerve, without any direct participation of the contractile substance. The proof lies in this. If the nerve of a sartorius be exposed as before, and a muscular section in the situation indicated be dipped into concentrated glycerine, contractions, at first fibrillar and very unlike those caused by true muscular irritants, will ensue. Let the ascending stream for the nerve now be closed; the muscle is at once tranquillized. If the circuit be again opened, the usual opening's contraction occurs, and at once passes into the glycerine contractions, which soon reach a perfect tetanus. Each of the other chemical excitants corresponds in its effects with what has been already advanced, no matter how varied the combination of muscle and nerve in the surface tested. Those sections which are near the nerve-trunk, further prove that the paralyzing influence of the constant stream at no point passes into the muscular tissue, and conversely, the distant sections show that the influence of the ascending stream reaches to the ultimate nerve fibrillæ. Thus the ascending stream is powerless over the irritability of the sarcous tissue, but renders the motor nerve insensible to its extreme ends. It is also hereby proved that the muscle propagates the excitation from transverse section to transverse section by its own substance, and without the agency of the nerves.

Many questions of moment are directly allied to these considerations. They afford data towards the determination of the ultimate distribution of nerve to muscle. The question of the retrograde or double sense conducting power of nerve tissue is also fairly opened. The varieties of muscular contraction admit of discussion, and the exact effects of Curari on muscle and nerve can be analysed. With all of these subjects Kühne has dealt more or less extensively. We will review them in the order here stated.

Rosenthal * ascertains that the motor nerve is more easily excited by slight oscillations than the muscle by direct electrical excitation. Hence a muscle with many intramuscular nerves will be more easily excited than one with few, and those parts of the muscle which are rich in nerves will more readily be induced to contract than those which are scantily supplied. The diminished irritability of the two terminal segments Kühne observes to be in remarkable harmony with the anatomical absence of nerves in these parts upon which he has already insisted. But can these phenomena be referred to the descending

* Op. cit.

curve of irritability of the motor nerve from centre to periphery? Were this the case the irritability of the muscle should gradually diminish in the form of this curve from the hilum to the extremities. Now careful observation with the Rheochord as a measure indicates a point of maximum irritability close to the hilum. In the immediate neighbourhood there is certainly a diminution, but then the intensity of current required remains pretty constant till near the termination of the muscle, so as not to represent a curve. When close upon the extremity the Rheochord suddenly indicates a great fall of irritability, and then the amount of excitation required remains uniform till quite the end of the muscle. Is the uniformity which is observed in the middle piece in contradiction with the undoubted curve of irritability which exists towards the cerebrum? Kühne considers the law to hold good, and accounts for the uniformity noted by the multiplication of the primitive nerve fibres increasing the points of attack. The sudden ultimate fall he ascribes to the total absence of nerves in the ends of the sartorius. He then tests this last hypothesis by means of the ascending constant stream. He so arranges a sartorius and its nerve that the constant ascending stream can be applied at will. The electrodes of the Rheochord apparatus are then applied to a central piece of the inverted sartorius, and the amount of new-silver wire, necessary to be introduced in order exactly to produce contraction, is measured. If these electrodes be then transferred to the extremity of the muscle it is found necessary to introduce nearly thirty centimetres of new-silver wire into the circuit in order to induce contraction. The electrodes are then restored to the neighbourhood of the hilum, and the new silver wire reduced, and the nerve is suddenly brought under the influence of the ascending stream. It will then be found necessary to introduce the same amount of new silver wire into the circuit to induce contraction as when the excitation was applied to the extremity of the muscle, and this intensity of stream will now be found uniform for the whole muscle. Thus all the differences between the various sections fall away as soon as the nerve is fairly paralysed by the ascending stream. The total irritability of the muscle is reduced by the electrotonic condition of the nerve, and a determinate minimum of irritation is found for the muscular tissue itself, contrary to the assertions of Eckhard, who appears to have only used the minimum stream for the nerve as a muscular excitant, whilst his nerve was in anelectrotone. It is probable that the minimum of irritation only affects the nerves of a nerve holding muscle. When the minimum is exceeded both organs are attacked. The minimum of exciting force for the muscular

tissue being thus ascertained we have a means of tracing the nervous distribution in the nerve-holding sections. If the electrodes be so closely opposed as only to include a few primitive fasciculi of the muscle, a quite local contraction of these few fasciculi alone will ensue. This is true both of the nerveless and nerve-holding sections. If a branch of nerve chance to be included, forcible contractions of a large tract or of the entire muscle will result. That a much diminished intensity of stream suffices to do this shows that the observer is dealing with the intramuscular nerve. Hence close to the entrance of the nerve trunk there are spots devoid of nervous tissue. Here, of course, it is impossible to imagine that the paralysing influence loses its energy owing to the remoteness of the immediately influenced spot.

We now pass on to the experimental evidence of the capacity of a motor nerve to conduct excitations as well towards the centres as from them, in other words to the capacity to carry stimuli in a double direction. Of the anatomical fact that the ultimate nerve fibres sub-divide we need give no proof. The object of experimentation is to demonstrate nervous retrograde conduction by means of muscular contraction. This might easily be decided if it were possible to isolate a secondary nerve-fibre and the muscular fasciculus corresponding to one limb of the bifurcation. Every contraction of the fasciculus on irritation of another branch of the parent nerve fibre were evidence that the latter carried the excitation upwards to the point of bifurcation, whence it descended to the muscle. This isolation can be effected physiologically by two methods. The contractile substance of a portion of the muscle may be destroyed by an agent which is incapable of injuring the nerve. There are many such: distilled water of 40° C, hydrochloric acid of 0·1 per cent., sulphocyanide of potassium of 1 per cent. Or the upper end of a sartorius may be dipped into oil of 40° C. The contractile substance coagulates, but the nerve for a while retains its conducting power. If sections be then made in the nerveless zone, between α and β no contractions follow, but if between β and γ (Plate X, fig. 2), very limited ones will ensue in that part of the muscle which has not been exposed to the re-agent. This may be confirmed by the use of the mineral acids, or of sulphate of copper which, being pure muscular excitants, cause no contractions, whereas glycerine and potash induce them. Still this is an uncertain experiment. A better method is to split the upper extremity of a sartorius longitudinally for 7—8 millimetres. All sections of the one limb that may be made below the line α fig. 3, cause contraction of the half of the muscle A soleiy, but

sections between *a* and B simultaneously cause fibrillar contractions in the half B. The chemical tests may be resorted to as above for confirmation. It will then be found that pure muscular irritants engender contractions only in those fibres to which they are applied; to induce contraction in the other segment of the muscle nerve excitants must be employed. It might be objected that the contraction which is carried from one part of the muscle to another was to be ascribed to an excitation of the nerves by means of the negative stream oscillation caused by the contraction of the directly irritated muscular fibres. Now it is certainly true that the muscle evinces the negative stream oscillation both on direct mechanical and on chemical excitation, because secondary contractions of a rheoscopic muscle can be obtained by means of it. But the negative oscillation of the muscular stream is an irritant that can only affect very excitable nerves. Thus it is only possible to propagate the contraction of one sartorius to another muscle if the sciatic plexus be employed. The lower parts of the sciatic nerve are not sufficiently irritable. Hence a muscle during contraction cannot excite its own nerve, as the negative oscillation of its stream impinges upon the nerve at the point where it is least excitable. The circumstances that all excitations of the nerveless terminal zone only act on the fibres irritated, and further that even in the nerve-holding region nerve excitants alone suffice to evoke contractions in the not directly excited fibres clearly show that we have not to deal with mechanical draggings by means of which the contracting part of the muscle could excite the nerves of the not directly irritated parts. It has further been objected that this contraction of both halves of the muscle depended on the formation of a double loop of nerve. This can be experimentally disproved. If the nerve of a muscle thus prepared be laid over the electrodes of a constant battery and transverse sections be laid on the one limb of the split, a point will be reached when the other half will also contract. Let the circuit of the battery be now closed so as to put the nerve into anelectrotone; a fresh section will only cause contraction of the fibres divided. If the stream be again opened, a fresh section will cause contraction of both halves. Now, presuming a loop to exist, after it had been divided the distal piece of nerve could not be affected by the anelectrotone. The incision would, at the same time, act as a stimulant and remove it from the influence of the anelectrotonic centre (Plate X, figs. 4 and 5). This can be further proved by a converse experiment. Let the split be advanced to near the hilus, where there are many nerve loops. Then divide the one limb close to the point of bifurcation. Contraction

of the opposite limb will always occur, whether the nerve be exposed to the ascending stream or not. The same holds of chemical excitants. If the one section be dipped into concentrated glycerine, contraction occurs in both halves of the muscle. If the paralysing stream be now closed, it ceases in both. Thus it can only be by branching of the primitive nerve fibres that the irritation can be conveyed. This method of experiment Kühne used as a test for the whole series of his chemical excitants, and found his previous observations confirmed.

The subject of the varieties of muscular contraction is one well worthy of attention. Schiff, who has laboured to a considerable extent in the same field as our author, has recently attempted to discriminate between the contractions which result from nervous excitation and those due to direct irritation of the muscle. He designates as neuro-muscular a contraction which extends from end to end of the muscular fasciculus and which may be excited primarily either by direct or by nervous irritation. This form of contraction he takes to be the one paralysed by the constant ascending stream. He regards as idio-muscular a contraction strictly confined to the site of irritation. "A small tumour arises which may last for several minutes as a persistent, tonic contraction. It is always slow and never pervades a whole fibre. Idio-muscular contractions are never induced by the galvanic stream, whilst chemical or mechanical excitation causes them strongly."* Certain *primâ facie* objections meet this interpretation. It assumes that the contractile substance is devoid of the power of conduction. The contraction following excitation of the nerve would require to be thought excited at all points simultaneously. Now, with the facts already discussed, this must either involve an effect in distans, beyond the material limit of the nerve, or the evoked contraction must be of so peculiar a character that only when it is called into being is the excitation capable of propagation to every consequent point of the contractile substance. Again, in direct electrical excitation, the intramuscular nerve alone is excited when the minimum of electricity is employed. If this minimum be exceeded by a certain determinate amount, paralysis of the nerve by the constant stream does not neutralize contraction. It may, however, be doubtful whether the electrical stream has acted directly on the contractile substance, or whether the paralysing influence on the nerve-trunk has only sufficed to reduce the irritability to a certain uniform level. To solve this question Kühne cut a sartorius into square

* Physiologie, pp. 21—24.

blocks, and opposed these by their cut surfaces, placing the two external ones in contact with the blotting-paper electrodes. The minimum of electricity, which admits of estimation by the induction coil, or by the Rheochord apparatus, will always cause only one segment, viz., that which contains the nerve-trunk, to contract. If the irritation be then increased, the piece next the hilus contracts, and lastly the pieces opposed to the electrodes. If these last pieces exclusively be employed, this last intensity of stream will be that which will induce them to contract. The author thus vindicates the individual character of muscular contractility and its faculty of propagation from section to section of the sarcous tissue. He is inclined to restrict the terms neuro and idio-muscular to those contractions that can be induced severally by indirect or by direct excitation. In both the contraction propagates in every direction within the sarcolemma.

Still that local spasm, which Schiff regards as idio-muscular, really exists, and it is necessary to have an exact idea of its nature. When a certain number of primitive fibres are irritated, say, by a needle being drawn transversely across them, they instantly contract in their whole length. When this true contraction has subsided, the site pressed upon gradually rises above the level of the surrounding muscle, so as to constitute a blunt mound exactly corresponding to the line of pressure, and which gradually disappears. Schiff has placed this contraction on a level with *rigor mortis*.

But Czermak has shown that a frog's thigh, whose nerve touches on the one hand the quiescent muscle, and on the other this idio-muscular tumor, passes over into secondary contraction; and this Kühne confirms. He has even found the same experiment to answer with warm-blooded animals. It might be inferred from this that the muscular stream at the excited point was either engaged in negative oscillation or in persistent decrease, and the experiment would be decisive for the question were it not certainly to be assumed that an absolute local destruction of the contractile substance would have precisely the same effect, inasmuch as the destroyed muscular substance could still serve as a conductor to the normal section of muscle in contact with it, so that the secondary contraction would only have the value of contraction without metal, of the contraction induced by the quiescent muscular stream. The fact, however, that these idio-muscular tumors can be repeatedly produced on the same spot argues that the secondary contraction which they bring about really is due to the negative oscillation of the muscular stream, although it remains a curious fact that no tetanic condition of the frog's thigh, analogous to

a secondary tetanus, should correspond to this permanent contraction. This last fact renders it probable that the permanent contraction, after mechanical irritation, represents the sole persistent muscular contraction as contrasted with the tetanus hitherto recognized. That it is totally distinct from *rigor mortis* is obvious, the phenomena of gradual disappearance and of reproduction even set aside, from the absence of all those signs that characterize rigor. A transverse section of such a tumor never has an acid re-action, and retains its transparency. Can we then bring this variety of contraction into conformity with that already discussed, and is it possible to abolish the use of the terms neuro and idio-muscular, as employed by Schiff, altogether? This is the view taken by Kühne. He remarks that Schiff has apparently overlooked the immense difference between the amount of irritation in a directly and in an indirectly affected spot. A strong analogy can be derived from nerve. A nerve can be destroyed at a given point by an irritation, but the spot adjacent to it may propagate the irritation without being also injured. The same holds of muscle, and it is not surprising that the muscle contracts more forcibly at the point where it is directly irritated than where one excited section serves as an irritant to the next. The appearance of the tumour subsequently to the general contraction depends upon the muscle being first pressed down by the irritant, and also requiring time to exceed the contraction by which the whole muscle has added to its thickness whilst in the quiescent state.

Schiff has further referred to the occurrence of a peculiar form of muscular contraction as the result of mechanical irritation of muscle, a considerable time after the death of the animal. If a sharp instrument be run across fibres that are no longer at the acmè of irritability a beautiful series of waves will run along the fasciculi in both directions. As the directly irritated spot rises to form a tumor, waves of contraction emanate from it, run to the end of the muscle and thence return. That this is a modified contraction is evident from its capacity to induce secondary contraction in a rheoscopic thigh. As the muscle dies these changes become more decided. The tumors are lower, occur later and last longer. But the contractions emanating from them undergo a similar change, so that a wave-like contraction can only be regarded as a slower form of the usual muscular contraction. At a last stage the idio-muscular tumor was itself seen by Kühne to divide into two slowly diverging waves of contraction. How then comes the idio-muscular tumor to be formed? The method of irritation affords the key to this. The more a muscle is fatigued, the easier is idio-muscular tumor obtained, and the

fatigue is proportionate to the amount of violence applied. In each experiment the site of irritation is fatigued, and hence the contraction which there ensues assumes an exhausted character, *i.e.*, occurs later and lasts longer. If the exciting medium be electricity, and the electrodes fine points, nodules will arise directly beneath them immediately after the contraction corresponding to the closure of the circuit has taken place. If this stream be passed transversely across a number of fasciculi only those directly under the electrodes contract. The density of steam does not suffice to excite the intermediate fibres, although at the points of contact it may be considerable. The fibres close to the electrodes, however, contract in their entire length; but at the electrodes the second condition, fatigue occurs, and a local, persistent contraction results. As the muscle dies out a wave of contraction may only start from the one pole, or the persistent contraction may only occur at one pole. It is probable that the products of electrolysis at the negative pole are active at a time when those at the positive pole have ceased to have any exciting power.

To sum up Kühne's arguments in favour of the individual character of muscular irritability they may be grouped thus:

I. Contraction of the muscle on direct irritation during palsy of the nerve by the ascending stream, the anelectrotonic nerve being inaccessible to chemical agents.

II. The contraction of the muscle on irritation of sections devoid of nerves.

III. The peculiar character of the contraction on the local application of such irritants to individual fibres as only act on the sarcous tissue.

IV. The difference of the contraction after local excitation when the extreme end of the intramuscular nerve is simultaneously excited, which rests on the capacity of the motor-nerve fibre to conduct in a double direction.

We have found Kühne asserting that it was not possible to determine this question by means of Curari. It remains for us to give an outline of what he holds to be the actual working of that poison. We will first consider its influence on the nerves which lie within the muscle. We have seen how the author disposed of the "local" contractions after poisoning described by Kölliker. Haber, also, we have noticed as speaking of a variety of "local" contraction different from that observed by Kölliker, inasmuch as, although limited to the fibres excited, it ran along their entire length. But we have also seen how these local contractions could be induced in unpoisoned muscles. Let us now refer back to the curve of excitability of the intramuscular nerve, the maximum point of which is at the entrance

of the nerve, and which gradually sinks as the nerve is distributed. We have seen that sudden palsy by anelectrotone could reduce the muscular irritability to a point below any existing along the curve of excitability. We thus know how a muscle should behave according or not as its nerve participates in a given irritation. This is a clue to determine the paralysing intensity of Curari. But first it is necessary, by a comparative experiment, to define the extent to which Curari poisoning reduces the irritability of nerve. Kühne drew a ligature round the iliac artery of one thigh, and another under the artery and sacral plexus, round the animal. Thus the access of poisoned blood to the one limb was prevented. He then poisoned the animal, and next drew corresponding ligatures round the opposite limb. This precaution is necessary in order to render the results strictly comparable. The muscles of the poisoned limb were found less irritable than those of the unpoisoned one; and this difference was most marked at the hilus. The nerveless zones, on the other hand, yielded perfectly uniform results. He, however, found the same distinction between sections rich in nerves and those poor in nerves, in the poisoned as in the unpoisoned muscles. This was true, whether tetanizing with the induction coil, or the closing contraction of the stream with the constant chain, when the Rheochord is the measure, be employed. Or the muscles might be excited by being divided into corresponding sections, the whole being laid on paper moistened with syrup of ·05 strength, so as to be simultaneously excited by the same intensity of stream. Thus, a muscle poisoned by Curari behaves like a normal muscle in all respects except that the differences between the various sections are smaller.

We now come to compare a poisoned muscle with one deprived of its nerve by anelectrotone. Two muscles, one of which is previously poisoned as above indicated, are so arranged that their hilus shall be close to the electrodes of an exciting battery; the nerve of the unpoisoned one—say the left,—is moreover carried over the zinc electrodes of a strong six-celled Grove's chain, by which an ascending stream can be passed through it. The relative irritability of the two muscles being previously tested, and that of the left being found greatest, the ascending circuit on its nerve is closed. Closure of the exciting weak chain will now only cause contraction of the right poisoned muscle, whilst the left, which previously contracted powerfully, remains at rest, or only contracts when greater resistances are introduced into the Rheochord. Now, as the latter has the relations of a muscle devoid of nerve, the conclusion is, that the poisoned muscle, whose contractile sub-

stance is on the same footing, retains a certain portion of nerve force which has been spared the action of the Curari. Kühne now raises an objection to his own experiment. The poisonings had only lasted for a few minutes. What other changes might occur on a longer contact with the poison?

We have seen glycerine, in the undiluted condition, to be a constant nerve-excitant; if the muscle contain any active nerve-tracks, these should be accessible to it. But here Kühne found himself at fault. After poisoning the application of glycerine to the first nerveless section caused contraction. The pure contractile substance behaved otherwise after poisoning than before. But another test presented itself to the author. A saturated solution of cane-sugar in water, when applied to the nerve, caused the most violent contractions, ending in a decided tetanus. Applied to a nerveless section, it evoked no contraction. In a nerve-holding section it caused a tetanus which the rapid application of anelectrotone could remove. A muscle poisoned with Curari behaves in its nerveless sections like a normal one. Here, then, the difficulty presented by the glycerine does not exist. Kühne now found that when the poisoned nerve-holding sections were dipped into the syrup, contractions ensued, although less forcibly than in unpoisoned sections. They were also restricted to individual fibres. This receives its explanation from the fact that an excited nerve-termination can only influence the fasciculi which pertain to it; whilst, in healthy nerve, every excitation of a peripheral end can affect many muscular fasciculi by centripetal conduction and transference by means of divided primitive nerve-fibres. Advancing a step further, can Curari ultimately affect the final terminations of the nerves? This is actually the case. A poisoning with 0·001 gr. of Curari—a maximum dose,—induces it in about two and a-half hours. This, however, is naturally quite inapplicable to explain the absence of contractions on irritation of the nerve-trunk immediately after poisoning. For this it is necessary to examine the influence of Curari on the motor-trunks.

The experiments of Bernard and Kölliker led to the assumption that paralysis advanced from periphery to centre; and it remained to be ascertained if Curari could affect the nerve-trunks when not applied through the capillaries of the muscle. Our limited space obliges us to pass over the experiments of Kölliker and the objections of Funke, till we find the latter analysing the electromotor relations of the nerve-trunks of poisoned frogs. These he found identical with those present in the normal nerve, *i. e.*, the quiescent nerve-stream, the two phases of electrotone; and lastly, on irritation, the negative

e.—Shows that not only does the germinal matter undergo conversion into cartilage at its external surface but that this alteration may occur as well in *the central part*.

f, g.—Show the same change in a still greater degree.

h.—Marks the position originally occupied by the germinal matter of cartilage, but this substance has entirely undergone conversion into matrix. The nucleus is dead and is therefore no longer coloured with carmine.

Fig. 16. Is a thin section through the temporary cartilage of the os calcis with the periosteum and tendon inserted into it. *a.*—Is the cartilage. The masses of germinal matter result from division, and some are seen actually undergoing the process, but in all cases the resulting masses are at once separated from each other. *b.*—Corresponds to the periosteum. Here stellate masses of germinal matter are observed, the processes of which are continuous. These also result from the division of masses of germinal matter but unlike those of cartilage, the resulting masses remain for some time continuous with each other. *c.*—Marks the tendon in which the masses of germinal matter are continuous but arranged linearly and not in the form of stellate masses as in the periosteum. *a.* near the centre of the figure marks a capillary vessel.

Fig. 17. Shows the structure and mode of development of cartilage in the mouse, and illustrates the manner in which fatty matter is deposited in the 'cells.' From the ensiform appendix of a young white mouse. The figures *a, b, c,* very much resemble those in the upper figure. *d.*—Germinal matter and nucleus with a small oil globule deposited in the germinal matter. *e.*—The same, but the oil globule has increased in size. *f.*—A further stage of the same change. The germinal matter and the nucleus are now seen lying between the globule of fatty matter and the formed material (wall of the cartilage cell). This is the position corresponding to that which the nucleus occupies in the fat vesicle and the primordial utricle in the 'starch-cell.'

Plate VII.

To illustrate the mode of formation of lacunæ and the process of calcification of bone. *Page* 82.

Fig. 18. Thin section of recently-formed bone with the periosteum. From the femur of a kitten one day old. *a.*—Areolar connective tissue on the outer part of the periosteum. *b.*—More compact tissue. In both these portions stellate masses of germinal matter are seen connected together by processes. These are usually termed connective tissue corpuscles. Capillaries are seen in this part of the drawing and numerous nuclei connected with their walls. *c.*—Is the inner layer of the periosteum, and here oval elementary parts can often be isolated. In fig. 44 these are represented much more highly magnified. As these grow, the soft-formed material increases, and the distance between the nuclei of these elementary parts of course becomes greater. *d.*—Shows the manner in which the formed material of the above becomes calcified. The calcareous matter is deposited in the oldest part of the formed material, and gradually increases from without inwards, towards the nucleus. Thus each nucleus becomes enclosed in a space, and the space gradually becomes less until the calcareous matter extends very close to the lacuna. The calcareous matter is doubtless incorporated with the matrix, and during this process, spaces are left which become the canaliculi. *e.*—Shows how the further deposition of calcareous matter takes place, and gives to the space a stellate appearance, which increases until the lacuna assumes its perfect characters.

Fig. 19. Elementary parts from the inner part of the periosteum marked *c* in the last figure.

Fig 20. A small lacuna in process of formation. Globules of calcareous matter are seen still retaining their spheroidal shape in some places, while in others the formation of the bone with the canaliculi is complete.

Fig. 21. A small lacuna still further from the periosteal surface almost perfectly formed.

Fig. 22. Two lacunæ from the femur of the kitten.

Fig. 23. Two lacunæ in the recently formed bone of the femur of the kitten. The germinal matter has undergone division, and a number of small elementary parts have been produced. These are increasing at the expense of the inner part of the lacuna. Thus the space gradually increases in size and becomes filled with small granular bodies. Several of these enlarged lacunæ run together and ultimately a space of considerable size results and the little granular 'cells' become the narrow cells which occupy the space.

Fig. 24. Cancellated structure from the first phalanx of the great toe of a girl about 16 years of age. *a*.—Portion of fully-formed bone. About the central part of the figure it would appear that the bone is being gradually removed. To the right a lacuna is being formed. Globules of calcareous matter are still seen, and immediately below, on a line with *b* several elementary parts are observed which have not yet undergone the process of calcification. *c*.—A capillary vessel with nuclei in its walls. Close to the vessel are oval masses of germinal matter surrounded with soft formed material. At *d* this formed material exhibits a fibrous character. *e*.—Large bodies composed of several elementary parts in process of growth. *f*.—Is growing in a curve. These are the so-called myeloid cells. They may become calcified and thus take part in the development of the spiculæ of bone which exist as imperfect septa between the cancelli. The nuclei in these masses, which are in a state of active growth, are tinged of a much darker colour by the carmine than those around them.

Plate VIII.

To illustrate the formation of the lacunæ of bone and the 'tubes' of dentine. Pages 82, 87.

Fig. 25. Cartilage of the temporal bone of an adult frog prior to ossification. Two of the masses of germinal matter

are undergoing division. The *septa* are not produced by the *growing in* of the matrix, but the outermost part of the germinal matter is converted into the so-called matrix.

Fig. 26. Another portion of the cartilage in which calcareous matter has been deposited. Globules of every size may be observed from the smallest visible particles to the large masses shown in the figure. The germinal matter is undergoing conversion into the formed material or matrix, and this is gradually becoming impregnated with calcareous salts. It must be borne in mind that the deposition of the calcareous matter always commences in the oldest portion of the formed material, which lies midway between the several masses of germinal matter.

Fig. 27. Shows a further stage of the process of calcification from the frontal bone of the frog.

Fig. 28. Two lacunæ from the frontal bone of the frog in process of formation. The spaces which are seen between the globules in this and in the last figure, gradually become narrower, and ultimately assume the characters of canaliculi.

Fig. 29. One third of the inner part of the wall of a fully formed lacuna near the periosteum. From the frog. A portion of the nucleus is represented in the lower part of the drawing to the right, and a number of separate globules are seen. These increase in number and size, and they coalesce at certain points and gradually encroach upon the nucleus. Magnified 1700 diameters.

Fig. 30. Two recently formed lacunæ and part of a third, from the frontal bone of the frog. The manner in which the canaliculi gradually become narrower proceeding in a direction *from* the nucleus, is well seen. As the lacunæ increase in age, the wide portions of the canaliculi which open into them gradually become contracted.

Fig. 31. A fragment of osseous tissue torn from perfectly formed bone from the frog. The canalicular tubes between the masses of calcareous matter are shown.

Fig. 32. Is a thin section of the inner portion of the dentine, and the surface of the pulp from an adult incisor *a*.—Where calcification is complete. To the right of this dark

portion the manner in which the calcareous matter is deposited in the matrix, is represented. Three distinct globules are seen. One of the so-called tubes traverses two of them. *b.*—Shows the uncalcified matrix or formed material. *c.*—Oval masses of germinal matter with formed material on their outer surfaces. *d.*—Terminal portions of nerve fibres.

The so-called tubes are seen to be occupied with soft processes which extend from the oval masses of germinal matter on the surface of the pulp, throughout the 'tubes.'

At *a* in the lower part of the figure one of these masses is torn out entire. It was continuous with the so-called matrix and would in great part have undergone calcification. It becomes much narrower as the tooth advances in age, and is always narrower at the outer part of the dentine which is the oldest portion, than near the pulp, which part was more recently formed. It is clearly solid.

Fig. 33. Transverse section of *uncalcified matrix* near the pulp. Notice the large size of the openings.

Fig. 34. *Calcified* matrix a little farther outwards.

Fig. 35. A fragment of dentine about the eighth of an inch from the inner part of the pulp cavity.

Fig. 36. Another fragment from about the same situation, in which several of the 'tubes' are obliterated by the increased deposition of calcareous matter in the matrix formed by the germinal matter which occupied the 'tube.'

Fig. 37. A section from the outer part of the dentine. The 'tubes' very narrow.

Plate IX.

To illustrate the structure of dentine, nervous ganglia and a tissue composed of 'stellate cells.' Pages 87, 89.

Fig. 38. A fragment of dentine near the pulp cavity with the prolongations of the masses of germinal matter in part of

their course still retained in situ. The prolongation of the germinal matter into the solid matter which occupies the 'dentinal tube' is well seen.

Fig. 39. One of the oval masses of germinal matter on the surface of the pulp with a small portion of the structure prolonged from it. This is surrounded by the matrix about to receive the calcareous deposit, only the inner part of which is torn away with the structure figured in the drawing. A number of small spherical particles are seen in the substance of the matter of which the contents of the 'dentinal tube' are composed $\times 2800$ diameters.

Fig. 40. One of the ganglion cells with nerve fibres connected with it from a nerve distributed to the pericardium of the ox. The large nucleus of the ganglion cell is seen, but in its substance, principally near the surface, a number of small oval nuclei resembling those in the nerves are also visible.

Fig. 41. A small portion of one of these 'ganglion cells' showing the continuity of the nerve fibre with the substance of the 'cell.'

Fig. 42. A portion of a ganglion on the side of a nerve showing ganglion cells and arrangement of the nerve fibres. Figs. 40 and 41 represent two of the 'cells' shown in this drawing more highly magnified.

Fig. 43. Tissue with stellate cells in immediate contact with the cementum of the fang of an incisor tooth. This is described under prep. 52, page 12. Towards the right of the drawing the 'cells' become smaller and the processes or tubes are seen to become narrower; then they appear solid and are lost in the matrix which is gradually becoming impregnated with calcareous particles.

Fig. 44. Muscular 'fibre-cells' from the circular coat of the aorta of a man who died from rupture of the arch. The tissue was torn if only very slight force was employed. These beautiful elementary parts with long radiating processes can hardly be called 'cells.' The processes are certainly fibrous. There is no possibility of distinguishing 'cell wall' and 'cell contents,' but the inner matter which is granular, gradually shades off into the fibrous substance of which the outer part of the processes is clearly composed.

The outer fibrous part of these elementary parts was not tinged by carmine; within this was a layer of tissue slightly reddened, and within this the colour was more intense, while the nucleus, which was situated *furthest* from the carmine solution, was very darkly coloured.

Plate X.

Illustrations to Dr. Eade's paper on diabetes insipidus. Page 127. *Dr. Duffin's abstract of Kühne's observations on muscular contraction, page* 141. *Casts of the seminal tubes found in urine. Page* 136.

Fig. 1. Kidney showing greatly dilated pelvis and calyces, shrunken pyramids, and diminished cortical portion.

Fig. 2. Sartorius muscle of the frog inverted, and partially dipped into oil of 40° centigrade, in order to destroy a portion of the contractile tissue without affecting the nerve fibres passing through the same. After Kühne. Page 153.

Fig. 3. Sartorius muscle of the frog split longitudinally, to prove centripetal conducting power of motor nerves. After Kühne. Page 153.

Figs. 4 and 5. Diagrams to illustrate the conclusion, arrived at from experiment, that centripetal conducting power really exists. P. 154.

Fig. 6. Spermatozoa in casts of the seminal tubules found in the urine of an old man aged 70.

Plate XI.

To illustrate arrangements of clinical microscopes for demonstrating objects to large classes. Apparatus designed by Mr. Hoblyn for pressing down thin glass cover while cements are drying. *Pages* 138, 140.

Fig. 1. Arrangement for showing eight preparations in microscopes which are all illuminated by a small French lamp placed in the centre. The names of the objects are written on ground glass slips inserted in the cover; and the objects can be measured by inserting a micrometer scale magnified in the same degree as the object itself by the side of the microscope.

Fig. 2 is the inside view of Fig. 1, and shows the manner in which the microscopes are retained in position. Each horizontal bar of wood can be screwed down upon two microscopes.

Fig. 3. Arrangement for holding four microscopes. The objects may be illuminated by lamps, or by ordinary daylight. A plate of glass is let into the cover; so that, with the aid of mirrors, the apparatus may be used in a room lighted with a skylight.

Fig. 4. Shows the manner in which the microscopes are maintained in their proper positions in fig. 3. *a* shows the position of the mirror, and *b* that of the lamp.

Fig. 5. Represents the arrangement by which various pieces of apparatus may be adapted to the clinical pocket microscope. *a* is the diaphragm. *b* is a sliding tube in which an achromatic or other form of condenser, prism, well, or stop, or polarising apparatus, is made to slide. *c* is the mirror. Each of these pieces is made to slide on a tube, and is prevented from slipping by a little screw.

Fig. 6. Apparatus designed by Mr. Hoblyn for pressing the thin glass on preparations while cements or Canada balsam are drying.

Fig. 15.

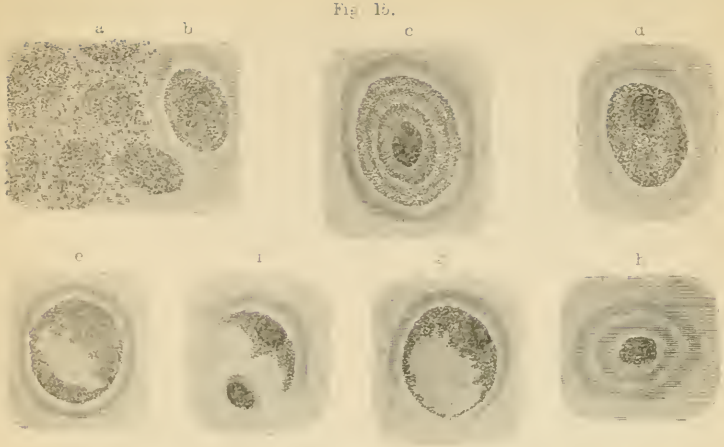
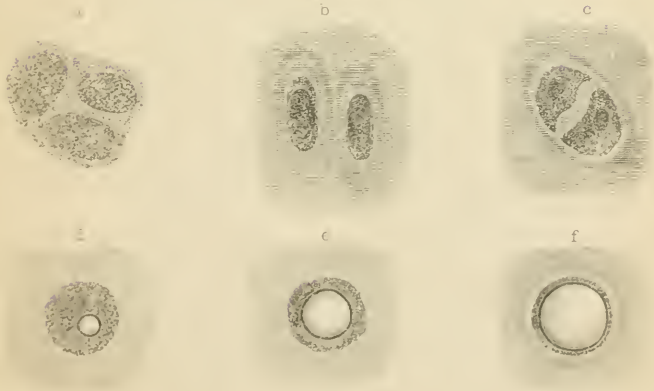


Fig. 16

Fig. 17.



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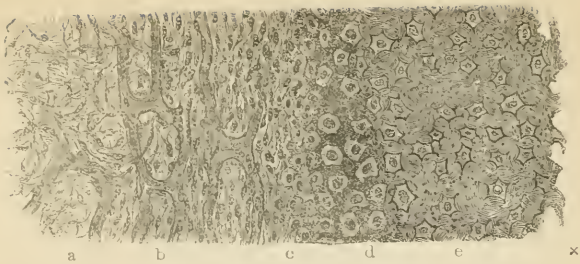

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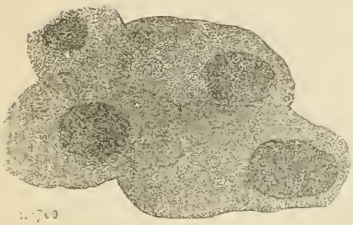

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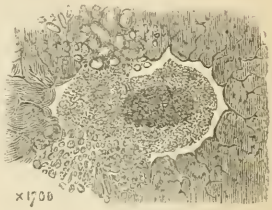

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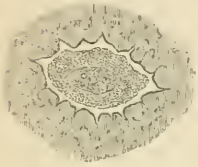

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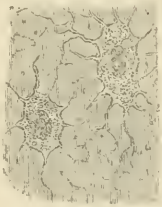

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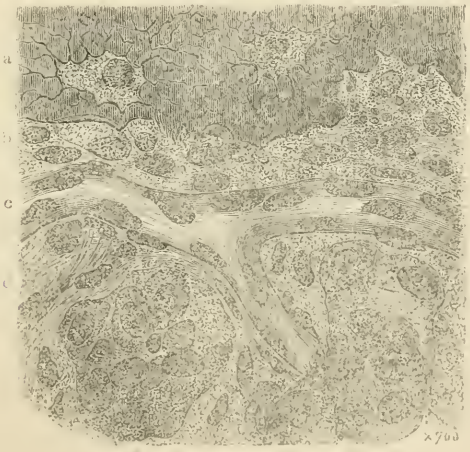

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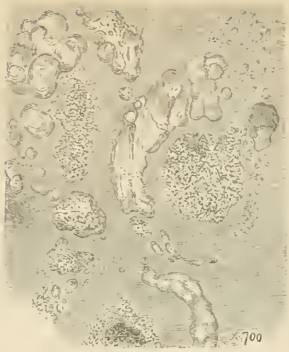

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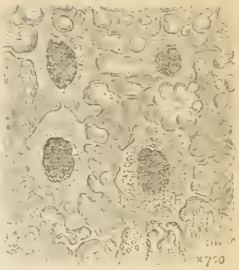

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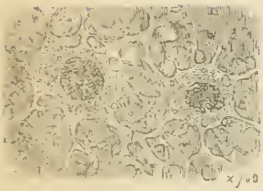

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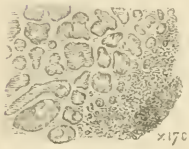

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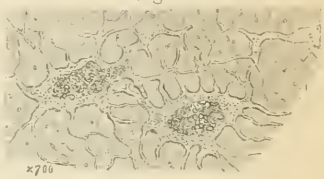

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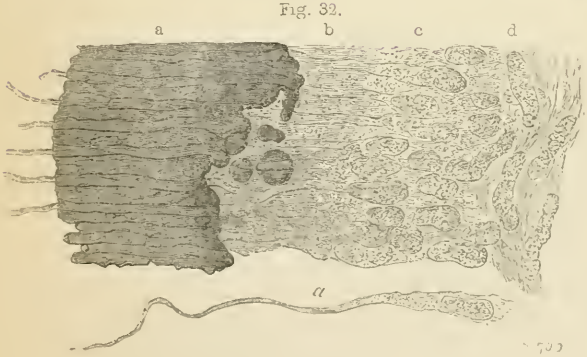

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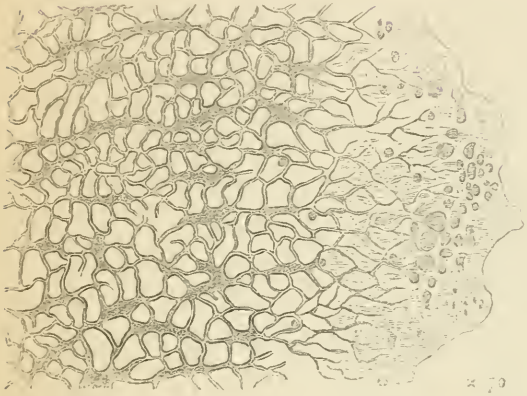

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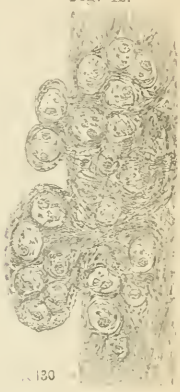

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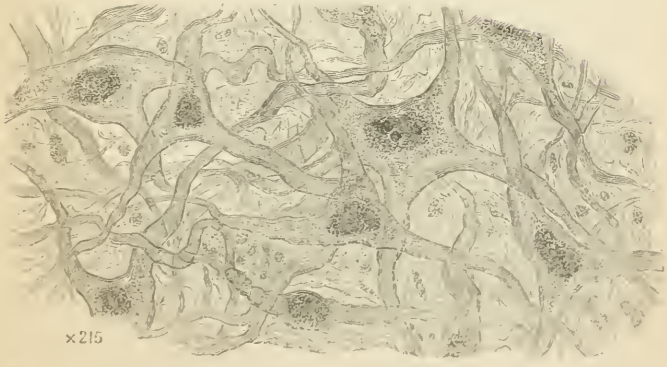

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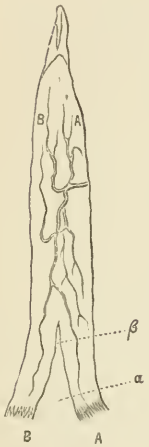

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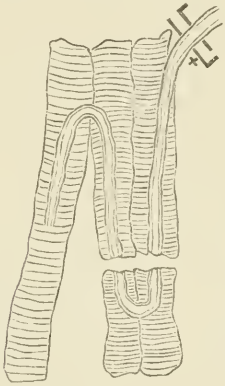

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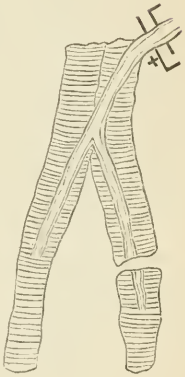

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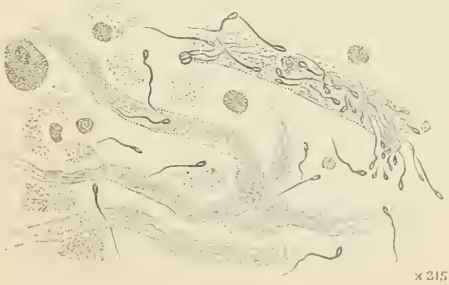

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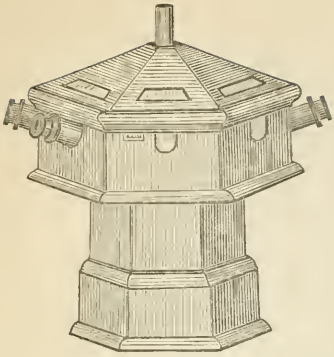

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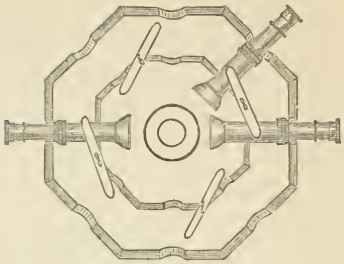

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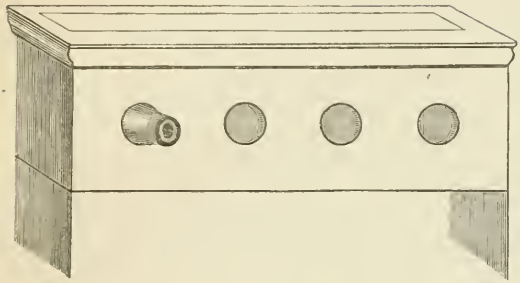

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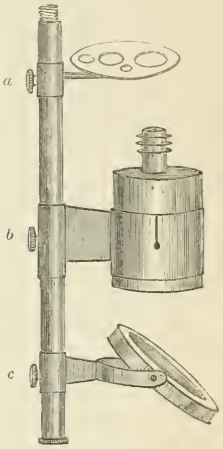

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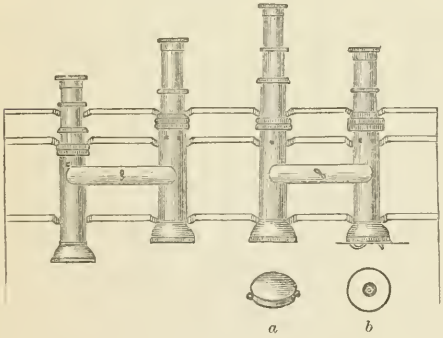

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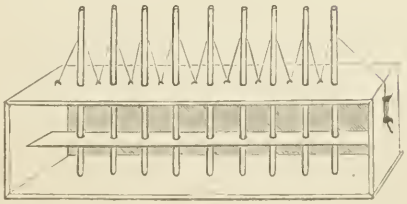

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III. Structure of a cancerous growth in the pharynx.

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XVI. To illustrate Dr. BEALE'S paper on a new form of pocket clinical microscope.

WOODCUTS

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II. ORIGINAL RESEARCHES IN ANATOMY AND PHYSIOLOGY, AND MORBID ANATOMY AND PATHOLOGY—

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On connective tissue, by Dr. Martyn.

On saccharine fermentation in the milk within the female breast, by Dr. Gibb.

On the action of chloroform upon the blood, by Dr. Sansom (Plate XIII).

On the occurrence of glucosuria in cases of burn, by Dr. Hill.

On the structure of tissues, with some observations on their growth, nutrition, and decay. 1. On the structure of some of the simplest living beings, and of the changes which occur during their life (Plate XV).

On the structure and growth of the tissues. A course of lectures, delivered at the Royal College of Physicians, by Dr. Beale.

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Plate XIII. Spermatozoa and casts from the seminal tubules,

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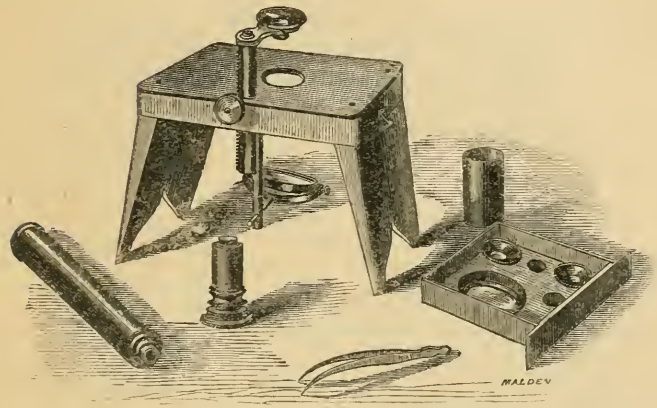

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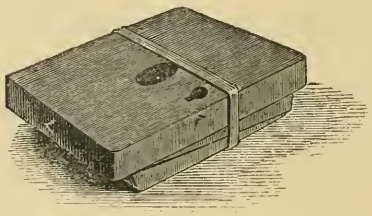

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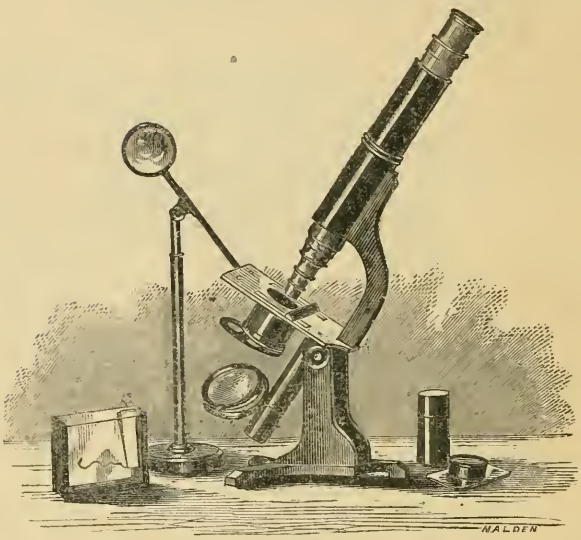

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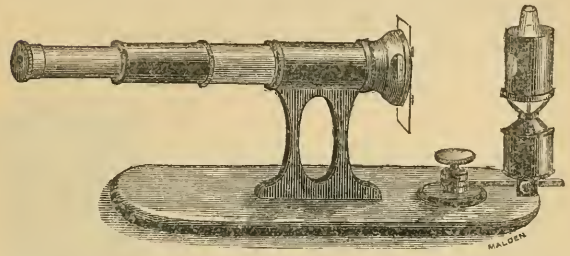

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*** *This combination of aquarium and microscope is specially arranged for* Sea Side Use, *but it also forms an elegant ornament for the study or drawing-room window. Object-glasses, Nos.* 2015, 2042, *or* 2093 *may be used with this instrument.*

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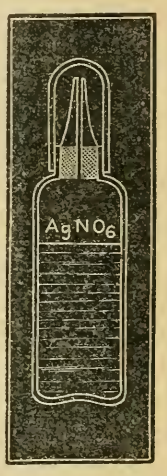
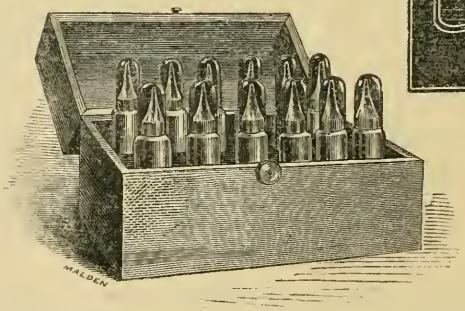
*** *This instrument is only made to order.*

2130. Apparatus for Examining Objects while exposed to the action of High Temperature. Fig.

HIGHLEY'S IMPROVED DROPPING BOTTLES for Microscopical Testing, &c., as described in the *Quarterly Journal of Microscopical Science*, Vol. IV., p. 286; and Beale's *How to Work with the Microscope*, p. 90. Fig. each 1*s.*





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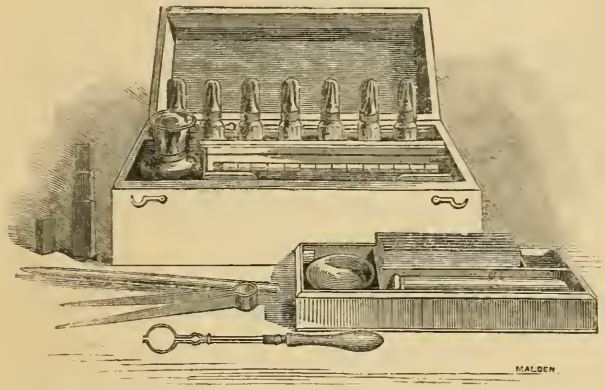

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No. XI (2s. 6d.), forming the third Number of Vol. III, will be published on March 3rd, 1862. Four numbers will be published in the year.

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